```
Connecting via Winsock to STN



Welcome to STN International!  Enter x:x

LOGINID:ssspta1653adk

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2


* * * * * * * * * * *   Welcome to STN International   * * * * * * * * * * *

 NEWS  1          Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2          "Ask CAS" for self-help around the clock
 NEWS  3  JAN 27  Source of Registration (SR) information in REGISTRY updated
                  and searchable
 NEWS  4  JAN 27  A new search aid, the Company Name Thesaurus, available in
                  CA/CAplus
 NEWS  5  FEB 05  German (DE) application and patent publication number format
                  changes
 NEWS  6  MAR 03  MEDLINE and LMEDLINE reloaded
 NEWS  7  MAR 03  MEDLINE file segment of TOXCENTER reloaded
 NEWS  8  MAR 03  FRANCEPAT now available on STN
 NEWS  9  MAR 29  Pharmaceutical Substances (PS) now available on STN
 NEWS 10  MAR 29  WPIFV now available on STN
 NEWS 11  MAR 29  New monthly current-awareness alert (SDI) frequency in RAPRA
 NEWS 12  APR 26  PROMT: New display field available
 NEWS 13  APR 26  IFIPAT/IFIUDB/IFICDB: New super search and display field
                  available
 NEWS 14  APR 26  LITALERT now available on STN
 NEWS 15  APR 27  NLDB: New search and display fields available
 NEWS 16  May 10  PROUSDDR now available on STN
 NEWS 17  May 19  PROUSDDR: One FREE connect hour, per account, in both May
                  and June 2004
 NEWS 18  May 12  EXTEND option available in structure searching
 NEWS 19  May 12  Polymer links for the POLYLINK command completed in REGISTRY
 NEWS 20  May 17  FRFULL now available on STN
 NEWS 21  May 27  STN User Update to be held June 7 and June 8 at the SLA 2004
                  Conference
 NEWS 22  May 27  New UPM (Update Code Maximum) field for more efficient patent
                  SDIs in CAplus
 NEWS 23  May 27  CAplus super roles and document types searchable in REGISTRY
 NEWS 24  May 27  Explore APOLLIT with free connect time in June 2004

 NEWS EXPRESS  MARCH 31 CURRENT WINDOWS VERSION IS V7.00A, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 26 APRIL 2004
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS INTER    General Internet Information
 NEWS LOGIN    Welcome Banner and News Items
 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
 NEWS WWW      CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that
specific topic.

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  of commercial gateways or other similar uses is prohibited and may
  result in loss of user privileges and other penalties.

  * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 08:49:08 ON 09 JUN 2004

=> file caplus biosis embase scisearch
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     1.89       1.89

FILE 'CAPLUS' ENTERED AT 08:54:42 ON 09 JUN 2004
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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE 'BIOSIS' ENTERED AT 08:54:42 ON 09 JUN 2004
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FILE 'EMBASE' ENTERED AT 08:54:42 ON 09 JUN 2004
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FILE 'SCISEARCH' ENTERED AT 08:54:42 ON 09 JUN 2004
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=> index caplus biosis embase scisearch
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     4.57       6.46

INDEX 'CAPLUS, BIOSIS, EMBASE, SCISEARCH' ENTERED AT 08:54:59 ON 09 JUN 2004

4 FILES IN THE FILE LIST IN STNINDEX

Enter SET DETAIL ON to see search term postings or to view
search error messages that display as 0* with SET DETAIL OFF.

=> s (dna or ?dna or rna) (p) (intercalat? or bind? or inhibit?) (p) (polyami? or alkylamin?) (p)
(base?pair or  minor?groove or major?groove)
          0*  FILE CAPLUS

=> set detail on perm
SET COMMAND COMPLETED

=> s (dna or ?dna or rna) (p) (intercalat? or bind? or inhibit?) (p) (polyami? or alkylamin?) (p)
(base?pair or  minor?groove or major?groove)\
MISSING OPERATOR OR?GROOVE)\
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s (dna or ?dna or rna) (p) (intercalat? or bind? or inhibit?) (p) (polyami? or alkylamin?) (p)
(base?pair or minor?groove or major?groove)\
MISSING OPERATOR OR?GROOVE)\
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s (dna or ?dna or rna) (p) (intercalat? or bind? or inhibit?) (p) (polyami? or alkylamin?) (p)
(base?pair or minor?groove or major?groove)
FILE 'CAPLUS'
'?DNA' NOT LONG ENOUGH FOR LEFT TRUNCATION
You have entered a truncated stem whose length is less than
the minimum allowed for left truncation in the requested
search field.  You may increase the length of the stem to
the minimum allowed and try again.  Enter HELP SFIELDS to
to find the minimum stem length for left truncation in
the requested search field.

=> s (dna or dsdna or rna) (p) (intercalat? or bind? or inhibit?) (p) (polyami? or alkylamin?) (p)
(base?pair or minor?groove or major?groove)
FILE 'CAPLUS'
'?' TRUNCATION SYMBOL NOT VALID WITHIN 'BASE?PAIR'
The truncation symbol ?  may be used only at the end of a search
term.  To specify a variable character within a word use '!', e.g.,
'womin' to search for both 'woman' and 'women'.  Enter "HELP
TRUNCATION" at an arrow prompt (=>) for more information.

=> s (dna or dsdna or rna) (p) (intercalat? or bind? or inhibit?) (p) (polyami? or alkylamin?) (p)
(basepair or base(a2)pair or minor(a2)groove or major(a2)groove)
MISSING OPERATOR 'BASE(A2'
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s (dna or dsdna or rna) (p) (intercalat? or bind? or inhibit?) (p) (polyami? or alkylamin?) (p)
(basepair or base(2a)pair or minor(2a)groove or major(2a)groove)
FILE 'CAPLUS'
       664722 DNA
        17068 DNAS
       667351 DNA
                (DNA OR DNAS)
         2749 DSDNA
           35 DSDNAS
         2761 DSDNA
                (DSDNA OR DSDNAS)
       271065 RNA
        21475 RNAS
       275003 RNA
                (RNA OR RNAS)
        38338 INTERCALAT?
      1045233 BIND?
      1659007 INHIBIT?
       199201 POLYAMI?
        25345 ALKYLAMIN?
          532 BASEPAIR
          397 BASEPAIRS
          872 BASEPAIR
```

```
              (BASEPAIR OR BASEPAIRS)
      599737 BASE
      139474 BASES
      685441 BASE
              (BASE OR BASES)
      208257 PAIR
      141685 PAIRS
      312871 PAIR
              (PAIR OR PAIRS)
      144723 MINOR
         239 MINORS
      144941 MINOR
              (MINOR OR MINORS)
       28043 GROOVE
       16529 GROOVES
       40144 GROOVE
              (GROOVE OR GROOVES)
      538758 MAJOR
        1072 MAJORS
      539689 MAJOR
              (MAJOR OR MAJORS)
       28043 GROOVE
       16529 GROOVES
       40144 GROOVE
              (GROOVE OR GROOVES)
         264 (DNA OR DSDNA OR RNA) (P) (INTERCALAT? OR BIND? OR INHIBIT?)
             (P) (POLYAMI? OR ALKYLAMIN?) (P) (BASEPAIR OR BASE(2A)PAIR OR
             MINOR(2A)GROOVE OR MAJOR(2A)GROOVE)
FILE 'BIOSIS'
     1032840 DNA
       11243 DNAS
     1034720 DNA
              (DNA OR DNAS)
      157573 DSDNA
          20 DSDNAS
      157577 DSDNA
              (DSDNA OR DSDNAS)
      719030 RNA
       16084 RNAS
      721929 RNA
              (RNA OR RNAS)
       10022 INTERCALAT?
      654228 BIND?
     1201150 INHIBIT?
       15536 POLYAMI?
        2341 ALKYLAMIN?
         681 BASEPAIR
         547 BASEPAIRS
        1153 BASEPAIR
              (BASEPAIR OR BASEPAIRS)
      148277 BASE
       34462 BASES
      174261 BASE
              (BASE OR BASES)
       69541 PAIR
       78032 PAIRS
      132533 PAIR
              (PAIR OR PAIRS)
      101842 MINOR
         294 MINORS
      102070 MINOR
              (MINOR OR MINORS)
        8806 GROOVE
        2801 GROOVES
       10953 GROOVE
              (GROOVE OR GROOVES)
    14806112 MAJOR
         402 MAJORS
    14806112 MAJOR
              (MAJOR OR MAJORS)
        8806 GROOVE
        2801 GROOVES
       10953 GROOVE
              (GROOVE OR GROOVES)
         138 (DNA OR DSDNA OR RNA) (P) (INTERCALAT? OR BIND? OR INHIBIT?)
             (P) (POLYAMI? OR ALKYLAMIN?) (P) (BASEPAIR OR BASE(2A)PAIR OR
             MINOR(2A)GROOVE OR MAJOR(2A)GROOVE)
FILE 'EMBASE'
      554811 DNA
        9248 DNAS
      555926 DNA
              (DNA OR DNAS)
        2176 DSDNA
          18 DSDNAS
        2180 DSDNA
              (DSDNA OR DSDNAS)
      292743 RNA
       14600 RNAS
      294189 RNA
              (RNA OR RNAS)
        7661 INTERCALAT?
      618208 BIND?
      994579 INHIBIT?
       11743 POLYAMI?
        1348 ALKYLAMIN?
         547 BASEPAIR
         434 BASEPAIRS
         924 BASEPAIR
              (BASEPAIR OR BASEPAIRS)
      150772 BASE
       26617 BASES
      169556 BASE
              (BASE OR BASES)
       46633 PAIR
       50736 PAIRS
       88743 PAIR
              (PAIR OR PAIRS)
       90469 MINOR
         736 MINORS
       91107 MINOR
              (MINOR OR MINORS)
        6851 GROOVE
        1589 GROOVES
        8055 GROOVE
              (GROOVE OR GROOVES)
     1665763 MAJOR
         207 MAJORS
     1665914 MAJOR
              (MAJOR OR MAJORS)
        6851 GROOVE
        1589 GROOVES
        8055 GROOVE
              (GROOVE OR GROOVES)
         140 (DNA OR DSDNA OR RNA) (P) (INTERCALAT? OR BIND? OR INHIBIT?)
             (P) (POLYAMI? OR ALKYLAMIN?) (P) (BASEPAIR OR BASE(2A)PAIR OR
             MINOR(2A)GROOVE OR MAJOR(2A)GROOVE)
FILE 'SCISEARCH'
      521500 DNA
        8780 DNAS
      524246 DNA
              (DNA OR DNAS)
        2278 DSDNA
          23 DSDNAS
        2286 DSDNA
              (DSDNA OR DSDNAS)
      287718 RNA
       30627 RNAS
      304636 RNA
              (RNA OR RNAS)
       23222 INTERCALAT?
      663576 BIND?
      895579 INHIBIT?
       25295 POLYAMI?
        3231 ALKYLAMIN?
         595 BASEPAIR
         428 BASEPAIRS
         970 BASEPAIR
              (BASEPAIR OR BASEPAIRS)
      194527 BASE
       48976 BASES
      233303 BASE
              (BASE OR BASES)
      105837 PAIR
       91642 PAIRS
      180662 PAIR
              (PAIR OR PAIRS)
       96584 MINOR
         868 MINORS
       97305 MINOR
              (MINOR OR MINORS)
       11374 GROOVE
        4444 GROOVES
       14733 GROOVE
              (GROOVE OR GROOVES)
      465014 MAJOR
         764 MAJORS
      465714 MAJOR
              (MAJOR OR MAJORS)
       11374 GROOVE
        4444 GROOVES
```

```
        14733 GROOVE
                (GROOVE OR GROOVES)
          188 (DNA OR DSDNA OR RNA) (P) (INTERCALAT? OR BIND? OR INHIBIT?)
              (P) (POLYAMI? OR ALKYLAMIN?) (P) (BASEPAIR OR BASE(2A)PAIR OR
              MINOR(2A)GROOVE OR MAJOR(2A)GROOVE)

L1   QUE (DNA OR DSDNA OR RNA) (P) (INTERCALAT? OR BIND? OR INHIBIT?) (P) (POLY
       AMI? OR ALKYLAMIN?) (P) (BASEPAIR OR BASE(2A) PAIR OR MINOR(2A) GROOVE
       OR MAJOR(2A) GROOVE)

=> analyze l1
THIS COMMAND IS NOT AVAILABLE IN STNINDEX
Some commands are not allowed after the INDEX command.  Enter HELP
COMMANDS at an arrow prompt (=>) for a list of commands that may be
used in STNINDEX.

=> file caplus biosis embase scisearch
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                                 9.69      16.15

FILE 'CAPLUS' ENTERED AT 09:04:57 ON 09 JUN 2004
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FILE 'SCISEARCH' ENTERED AT 09:04:57 ON 09 JUN 2004
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=> s l1
   3 FILES SEARCHED...
L2          730 L1

=> analyze l2
ENTER ANSWER NUMBER OR RANGE (1-):1-703
ENTER DISPLAY CODE (FILEDEFAULT) OR ?:end

=> analyze l2 1-730
ENTER DISPLAY CODE (FILEDEFAULT) OR ?:
ENTER DISPLAY CODE (FILEDEFAULT) OR ?:?
Enter a display code to select on.
AB    ------ Abstract Text
AC ------ Patent Application Country
AD ------ Patent Application Date
AI ------ Patent Application Information
AN ------ Accession Number
AP ------ Patent Application Number
APPS ----- Patent Application and Priority Number
AU ------ Author or Patent Inventor
AY ------ Patent Application Year
CC ------ CA Classification Codes
CK ------ Crossover Key
CS ------ Corporate Source or Patent Assignee
CS.DIV -- Corporate Source, Division
CS.ORG -- Corporate Source, Organization Name
CT ------ Controlled Term
CYA ----- Country Name of Author
DS ------ Designated States (Patents)
DT ------ Document Type
FAN ----- Family Accession Number
FS ------ File Segment
GENBANK - GENBANK Number
IC ------ International Patent Classification (IPC)
ICA ----- Additional (Supplementary) IPC
ICI ----- Index (Complementary) IPC
ICM ----- Main IPC
ICS ----- Secondary IPC
IN ------ Inventor Name
ISN ----- International Standard (Document) Number
ISSN----- ISSN
IPC ----- International Patent Classifications
IT ------ Index Entries
JT ------ Journal Title
LA ------ Language
NCL------ National Patent Classification Code
OS ------ Other Source
PA ------ Patent Assignee
PATS----- Patent Numbers
PC ------ Patent Country
PCS ----- Patent Countries
PD ------ Publication Date
PI ------ Patent Information
PK ------ Kind of Patent
PN ------ Patent Number
PRAI ---- Patent Priority Information
PRC ----- Patent Priority Country
PRD ----- Patent Priority Date
PRN ----- Patent Priority Number
PRY ----- Patent Priority Year
PY ------ Publication Year of Original Document
RE ------ Reference
REC ----- Reference Count
RAN.CA -- Reference CA File Accession Number
RAN.CAPLUS --- Reference CAPLus File Accession Number
RAN.MEDLINE -- Reference MEDLINE File Accession Number
RAN.ALL ------ Reference Accession Numbers for All Files
RIN ----- Reference Inventor
RAU ----- Reference Author
RWK ----- Reference Work
RPG ----- Reference Page Number
RPN ----- Reference Patent Number
RPY ----- Reference Publication Year
RVL ----- Reference Publication Volume
RL ------ Roles
RN ------ CAS Registry Number
SO ------ Source
ST ------ Supplementary Terms (CA Keywords)
SX ------ Chemical Abstract Section Cross-Reference Code
TI ------ Title of Document
ENTER DISPLAY CODE (FILEDEFAULT) OR ?:pd
L3          ANALYZE L2 1-730 PD :     355 TERMS

=>

=> d l3
L3          ANALYZE L2 1-730 PD :     355 TERMS

TERM #   # OCC  # DOC  % DOC PD
------ ------ ------ ------ ----------------
     1     21     21   2.88 1996/PD
     2     18     18   2.47 1997/PD
     3     12     12   1.64 1993/PD
     4      9      9   1.23 1991/PD
     5      9      9   1.23 2001/PD
     6      8      8   1.10 2002/PD
     7      7      7   0.96 2000/PD
     8      7      7   0.96 20000718/PD
     9      7      7   0.96 20031021/PD
    10      7      4   0.55 20000323/PD


=> d his

     (FILE 'HOME' ENTERED AT 08:49:08 ON 09 JUN 2004)

     FILE 'CAPLUS, BIOSIS, EMBASE, SCISEARCH' ENTERED AT 08:54:42 ON 09 JUN
     2004

     INDEX 'CAPLUS, BIOSIS, EMBASE, SCISEARCH' ENTERED AT 08:54:59 ON 09 JUN
     2004
               SEA (DNA OR ?DNA OR RNA) (P) (INTERCALAT? OR BIND? OR INHIBIT?)
               ---------
              0*  FILE CAPLUS
               SET DETAIL ON PERM
               SEA (DNA OR ?DNA OR RNA) (P) (INTERCALAT? OR BIND? OR INHIBIT?)
               ---------
              0*  FILE CAPLUS
               SEA (DNA OR DSDNA OR RNA) (P) (INTERCALAT? OR BIND? OR INHIBIT?
               ---------
              0*  FILE CAPLUS
               SEA (DNA OR DSDNA OR RNA) (P) (INTERCALAT? OR BIND? OR INHIBIT?
               ---------
             264   FILE CAPLUS
             138   FILE BIOSIS
             140   FILE EMBASE
             188   FILE SCISEARCH
L1             QUE (DNA OR DSDNA OR RNA) (P) (INTERCALAT? OR BIND? OR INHIBIT?
               ---------

     FILE 'CAPLUS, BIOSIS, EMBASE, SCISEARCH' ENTERED AT 09:04:57 ON 09 JUN
     2004
L2          730 S L1
L3          ANALYZE L2 1-730 PD :     355 TERMS
```

```
=>
=> s l2 and py>=1999
L4          486 L2 AND PY>=1999

=> s l2 not l4
L5          244 L2 NOT L4

=> dup rem
ENTER L# LIST OR (END):5
5 IS NOT VALID HERE
The L-number entered has not been defined in this session, or it
has been deleted.  To see the L-numbers currently defined in this
session, enter DISPLAY HISTORY at an arrow prompt (=>).

=> dup rem l5
PROCESSING COMPLETED FOR L5
L6            98 DUP REM L5 (146 DUPLICATES REMOVED)

=> analyze l5 1- pd
L7          ANALYZE L5 1- PD :      81 TERMS

=> tabulate l7
DISPLAY AS GRID FORMAT (N), Y, OR ?:y
ENTER PRIMARY DISPLAY CODE OR (?):pd
ENTER SECONDARY DISPLAY CODE OR (?):end

=> tabulate
ENTER ANALYZE OR SELECT L# (L7):
ENTER ANALYZE OR SELECT L# (L7):l7
DISPLAY AS GRID FORMAT (N), Y, OR ?:y
ENTER PRIMARY DISPLAY CODE OR (?):?
Enter the display field code to be used as the primary term.
ENTER PRIMARY DISPLAY CODE OR (?):ogt 4
'OGT 4' IS NOT VALID HERE
Please specify a single display field code to be used as the primary
TABULATE term.
ENTER PRIMARY DISPLAY CODE OR (?):icm
ENTER SECONDARY DISPLAY CODE OR (?):py
DISPLAY PRIMARY (TOP 10), ENTIRE OR ?:top 10
PRIMARY SORT ORDER (CURRENT), DOC, ALPHA, OR ?:current
PRIMARY SORT DIRECTION (DEFAULT), A, D, OR ?:A
SECONDARY SORT ORDER (CURRENT), DOC, ALPHA, OR ?:
SECONDARY SORT ORDER (CURRENT), DOC, ALPHA, OR ?:.
SECONDARY SORT DIRECTION (DEFAULT), A, D, OR ?:.
A FEE WILL BE CHARGED.  PROCEED? (Y), N, OR ?:y
L7          ANALYZE L5 1- PD :      81 TERMS

NO TERMS MATCHED THE PRIMARY TERM CRITERIA

REFORMAT USING SAME DISPLAY FIELDS? (N), Y, OR ?:y
DISPLAY AS GRID FORMAT (N), Y, OR ?:y
EXCHANGE PRIMARY AND SECONDARY DISPLAY FIELDS (N), Y, OR ?:y
DISPLAY PRIMARY (TOP 10), ENTIRE OR ?:entire
PRIMARY SORT ORDER (CURRENT), DOC, ALPHA, OR ?:.
PRIMARY SORT DIRECTION (DEFAULT), A, D, OR ?:.
SECONDARY SORT ORDER (CURRENT), DOC, ALPHA, OR ?:.
SECONDARY SORT DIRECTION (DEFAULT), A, D, OR ?:.
L7          ANALYZE L5 1- PD :      81 TERMS

NO TERMS MATCHED THE PRIMARY TERM CRITERIA

REFORMAT USING SAME DISPLAY FIELDS? (N), Y, OR ?:end

=> d his

     (FILE 'HOME' ENTERED AT 08:49:08 ON 09 JUN 2004)

     FILE 'CAPLUS, BIOSIS, EMBASE, SCISEARCH' ENTERED AT 08:54:42 ON 09 JUN
     2004

     INDEX 'CAPLUS, BIOSIS, EMBASE, SCISEARCH' ENTERED AT 08:54:59 ON 09 JUN
     2004
               SEA (DNA OR ?DNA OR RNA) (P) (INTERCALAT? OR BIND? OR INHIBIT?)
              ---------
              0*  FILE CAPLUS
               SET DETAIL ON PERM
               SEA (DNA OR ?DNA OR RNA) (P) (INTERCALAT? OR BIND? OR INHIBIT?)
              ---------
              0*  FILE CAPLUS
               SEA (DNA OR DSDNA OR RNA) (P) (INTERCALAT? OR BIND? OR INHIBIT?
              ---------
              0*  FILE CAPLUS
               SEA (DNA OR DSDNA OR RNA) (P) (INTERCALAT? OR BIND? OR INHIBIT?
              ---------
             264   FILE CAPLUS
             138   FILE BIOSIS
             140   FILE EMBASE
             188   FILE SCISEARCH
L1             QUE (DNA OR DSDNA OR RNA) (P) (INTERCALAT? OR BIND? OR INHIBIT?
               ---------

     FILE 'CAPLUS, BIOSIS, EMBASE, SCISEARCH' ENTERED AT 09:04:57 ON 09 JUN
     2004
L2          730 S L1
L3          ANALYZE L2 1-730 PD :     355 TERMS
L4          486 S L2 AND PY>=1999
L5          244 S L2 NOT L4
L6           98 DUP REM L5 (146 DUPLICATES REMOVED)
L7          ANALYZE L5 1- PD :      81 TERMS

=> d fbib abs hitstr total
'TOTAL' IS NOT VALID FOR SmartSELECT L-NUMBER DISPLAYS
L7          ANALYZE L5 1- PD :      81 TERMS


Please specify how many terms you wish to display.
Valid responses are:

  ENTIRE      display all of the terms
  TOP n       where n refers to a number of terms (i.e. TOP 10)
  OGT n       display terms with occurrence counts greater than 'n'
  DGT n       display terms with document counts greater than 'n'
  %GT n       display terms with percentage counts greater than 'n'
  PGT n       display terms with percentage counts greater than 'n'
  m-n         display the terms specified  (e.g. 1-5)

=> d entire fbib abs hitstr total
'ABS' IS NOT VALID HERE

=> d rank l6
'FULL' IS NOT VALID IN THE CURRENT FILE
This option is not valid in the current file.  Enter the command
without the option at the arrow prompt (=>).  Or, first enter the
file in which the saved item created.  Then enter the command and
option at an arrow prompt in the file.

=> rank l6
PROCESSING COMPLETED FOR L6
L8            98 FOCUS L6 1-

=> d rank
F1          264   CAPLUS
F2          188   SCISEARCH
F3          140   EMBASE
F4          138   BIOSIS


=> d l6 1- fbib abs hitstr total
YOU HAVE REQUESTED DATA FROM 196 ANSWERS - CONTINUE? Y/(N):n

=> d his

     (FILE 'HOME' ENTERED AT 08:49:08 ON 09 JUN 2004)

     FILE 'CAPLUS, BIOSIS, EMBASE, SCISEARCH' ENTERED AT 08:54:42 ON 09 JUN
     2004

     INDEX 'CAPLUS, BIOSIS, EMBASE, SCISEARCH' ENTERED AT 08:54:59 ON 09 JUN
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              ---------
              0*  FILE CAPLUS
               SET DETAIL ON PERM
               SEA (DNA OR ?DNA OR RNA) (P) (INTERCALAT? OR BIND? OR INHIBIT?)
              ---------
              0*  FILE CAPLUS
               SEA (DNA OR DSDNA OR RNA) (P) (INTERCALAT? OR BIND? OR INHIBIT?
              ---------
              0*  FILE CAPLUS
               SEA (DNA OR DSDNA OR RNA) (P) (INTERCALAT? OR BIND? OR INHIBIT?
              ---------
             264   FILE CAPLUS
             138   FILE BIOSIS
             140   FILE EMBASE
             188   FILE SCISEARCH
L1             QUE (DNA OR DSDNA OR RNA) (P) (INTERCALAT? OR BIND? OR INHIBIT?
               ---------

     FILE 'CAPLUS, BIOSIS, EMBASE, SCISEARCH' ENTERED AT 09:04:57 ON 09 JUN
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```

```
L2          730 S L1
L3          ANALYZE L2 1-730 PD :      355 TERMS
L4          486 S L2 AND PY>=1999
L5          244 S L2 NOT L4
L6           98 DUP REM L5 (146 DUPLICATES REMOVED)
L7          ANALYZE L5 1- PD :       81 TERMS
L8           98 FOCUS L6 1-

=> rem l7, l8
DELETE L7 L8? (Y)/N:y

=> d his

     (FILE 'HOME' ENTERED AT 08:49:08 ON 09 JUN 2004)

     FILE 'CAPLUS, BIOSIS, EMBASE, SCISEARCH' ENTERED AT 08:54:42 ON 09 JUN
     2004

     INDEX 'CAPLUS, BIOSIS, EMBASE, SCISEARCH' ENTERED AT 08:54:59 ON 09 JUN
     2004
               SEA (DNA OR ?DNA OR RNA) (P) (INTERCALAT? OR BIND? OR INHIBIT?)
               ---------
               0*  FILE CAPLUS
                SET DETAIL ON PERM
                SEA (DNA OR ?DNA OR RNA) (P) (INTERCALAT? OR BIND? OR INHIBIT?)
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               0*  FILE CAPLUS
                SEA (DNA OR DSDNA OR RNA) (P) (INTERCALAT? OR BIND? OR INHIBIT?
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               0*  FILE CAPLUS
                SEA (DNA OR DSDNA OR RNA) (P) (INTERCALAT? OR BIND? OR INHIBIT?
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              264   FILE CAPLUS
              138   FILE BIOSIS
              140   FILE EMBASE
              188   FILE SCISEARCH
L1               QUE (DNA OR DSDNA OR RNA) (P) (INTERCALAT? OR BIND? OR INHIBIT?
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     FILE 'CAPLUS, BIOSIS, EMBASE, SCISEARCH' ENTERED AT 09:04:57 ON 09 JUN
     2004
L2          730 S L1
L3          ANALYZE L2 1-730 PD :      355 TERMS
L4          486 S L2 AND PY>=1999
L5          244 S L2 NOT L4
L6           98 DUP REM L5 (146 DUPLICATES REMOVED)

=> d l6 1-98 ibib iabs

L6   ANSWER 1 OF 98  CAPLUS  COPYRIGHT 2004 ACS on STN DUPLICATE 1
ACCESSION NUMBER:         1998:411071  CAPLUS Full-text
DOCUMENT NUMBER:          129:132824
TITLE:                    Aliphatic/Aromatic Amino Acid Pairings for Polyamide
                          Recognition in the Minor Groove of DNA
AUTHOR(S):                Turner, James M.; Swalley, Susanne E.; Baird, Eldon
                          E.; Dervan, Peter B.
CORPORATE SOURCE:         Division of Chemistry and Chemical Engineering,
                          California Institute of Technology, Pasadena, CA,
                          91125, USA
SOURCE:                   Journal of the American Chemical Society (1998),
                          120(25), 6219-6226
                          CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER:                American Chemical Society
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
ABSTRACT:
Selective placement of an aliphatic β-alanine (β) residue paired
side-by-side with either a pyrrole (Py) or imidazole (Im) aromatic amino acid is
found to compensate for sequence composition effects for recognition of the
***minor***  groove of DNA by hairpin pyrrole-imidazole
***polyamides.***  A series of polyamides were prepared which contain
pyrrole and imidazole aromatic amino acids, as well as γ-aminobutyric acid
(γ) "turn" and β-alanine "spring" aliphatic amino acid residues.  The
***binding***  affinities and specificities of these polyamides are
regulated by the placement of paired β/β, Py/β, and Im/β
residues.  Quant. footprint titrns. demonstrate that replacing two Py/Py
pairings in a 12-ring hairpin (6-γ-6) with two Py/β pairings affords
10-fold enhanced affinity and similar sequence specificity for an 8-bp target
sequence.  The 6-γ-6 hairpin ImPyImPyPyPy-γ-ImPyPyPyPyPy-β-Dp,
which contains six consecutive amino acid pairings, is unable to discriminate a
single-base-pair mismatch site 5'-TGTTAACA-3' from a
5'-TGTGAACA-3' match site.  The hairpin polyamide
Im-β-ImPyPyPy-γ-ImPyPyPy-β-Py-β-Dp binds to the
8-bp match sequence 5'-TGTGAACA-3' with an equilibrium association constant of Ka =
2.4+1010 M-1 and ≥48-fold specificity vs. the 5'-TGTTAACA-3'
single-base-pair mismatch site.  Modeling indicates that
the β-alanine residue relaxes ligand curvature, providing for optimal
hydrogen bond formation between the floor of the minor groove
and both Im residues within the Im-β-Im polyamide subunit.  This
observation provided the basis for design of a hairpin polyamide,
Im-β-ImPy-γ-Im-β-ImPy-β-Dp, which incorporates Im/β
pairings to recognize a "problematic" 5'-GCGC-3' sequence at subnanomolar
concns.  These results identify Im/β and β/Im pairings that resp.
discriminate G·C and C·G from A·T/T·A as well as
Py/β and β/Py pairings that discriminate A·T/T·A from
G·C/C·G.  These aliphatic/aromatic amino acid pairings will facilitate
the design of hairpin polyamides which recognize both a larger
***binding***  site size as well as a more diverse sequence repertoire.

REFERENCE COUNT:          47    THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6   ANSWER 2 OF 98  CAPLUS  COPYRIGHT 2004 ACS on STN DUPLICATE 2
ACCESSION NUMBER:         1998:267278  CAPLUS Full-text
DOCUMENT NUMBER:          129:24618
TITLE:                    The theoretical limits of DNA sequence discrimination
                          by linked polyamides
AUTHOR(S):                Walker, Wynn L.; Landaw, Elliot M.; Dickerson, Richard
                          E.; Goodsell, David S.
CORPORATE SOURCE:         Department of Biomathematics and the Molecular Biology
                          Institute, University of California, Los Angeles, CA,
                          90024, USA
SOURCE:                   Proceedings of the National Academy of Sciences of the
                          United States of America (1998), 95(8), 4315-4320
                          CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER:                National Academy of Sciences
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
ABSTRACT:
Linked polyamides bind in the minor
***groove***  of double-stranded DNA in a partially
sequence-specific manner.  This report analyzes the theor. limits of
***DNA***  sequence discrimination by linked polyamides composed of
two to four different types of heterocyclic rings, determining (i) the optimal choice
of base-binding specificity for each ring and (ii) the optimal design
for a polyamide composed of these rings to target a given DNA
sequence and designed to maximize the fraction of the total polyamide
***binding***  to the specified target sequence relative to all other
sequences.  The results show that, fortuitously, polyamides composed
of pyrrole, a naturally occurring G-excluding element, and imidazole, a
rationally designed G-favoring element, have features similar to the theor.
optimum design for polyamides composed of two different rings.  The
results also show that, in polyamides composed of two or three types
of heterocyclic rings, choosing a nonspecific "placeholder" ring, which
***binds***  equally strongly to each of the four bases, along with one or two
base-specific rings will often enhance sequence specificity over a
***polyamide***  composed entirely of base-specific rings.

REFERENCE COUNT:          20    THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6   ANSWER 3 OF 98  CAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         1998:229729  CAPLUS Full-text
DOCUMENT NUMBER:          129:1795
TITLE:                    Recognition of 16 Base Pairs in the Minor Groove of
                          DNA by a Pyrrole-Imidazole Polyamide Dimer
AUTHOR(S):                Trauger, John W.; Baird, Eldon E.; Dervan, Peter B.
CORPORATE SOURCE:         Arnold and Mabel Beckman Laboratories of Chemical
                          Synthesis Division of Chemistry and Chemical
                          Engineering, California Institute of Technology,
                          Pasadena, CA, 91125, USA
SOURCE:                   Journal of the American Chemical Society (1998),
                          120(14), 3534-3535
                          CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER:                American Chemical Society
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
ABSTRACT:
Cell-permeable small mols. which bind predetd. DNA
sequences have the potential to regulate the expression of specific genes.
Recently, an 8-ring Im-Py polyamide which binds 6
***base***  pair sites as a hairpin was shown to inhibit
transcription of a specific gene in cell culture.  Polyamides
recognizing longer DNA sequences should provide more specific biol.
activity.  For the limiting case of recognition of a single site within the
3-billion base pair human genome, a ligand which
specifically recognizes 15-16 base pairs is required.  For
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this reason, recognition of 16 base pairs represents a milestone in the development of chemical approaches to DNA recognition. We report here that the 8-ring polyamide ImPy-β-ImPy-β-ImPy-β-PyPy-β-Dp (Im = N-methylimidazole, Py = N-methylpyrrole, β = β-alanine, and Dp = dimethylaminopropylamide) specifically binds the 16 base pair sequence 5'-ATAAGCAGCTGCTTTT-3' as a cooperative antiparallel dimer at subnanomolar concns. (Ka ≥ 3.5+1010 M-1). This result extends DNA recognition by Im-Py ***polyamides*** to 16 base pairs.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 98 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 1998:821419 SCISEARCH Full-text
THE GENUINE ARTICLE: 130VF
TITLE: Strong, specific, reversible binding ligands for transfer RNA: Comparison by fluorescence and NMR spectroscopies with distamycin binding for a new structural class of ligand
AUTHOR: Bichenkova E V; SadatEbrahimi S E; Wilton A N; OToole N; Marks D S; Douglas K T (Reprint)
CORPORATE SOURCE: UNIV MANCHESTER, SCH PHARM & PHARMACEUT SCI, MANCHESTER M13 9PL, LANCS, ENGLAND (Reprint); UNIV MANCHESTER, SCH PHARM & PHARMACEUT SCI, MANCHESTER M13 9PL, LANCS, ENGLAND
COUNTRY OF AUTHOR: ENGLAND
SOURCE: NUCLEOSIDES & NUCLEOTIDES, (29 SEP 1998) Vol. 17, No. 9-11, pp. 1651-1665. Publisher: MARCEL DEKKER INC, 270 MADISON AVE, NEW YORK, NY 10016. ISSN: 0732-8311.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 40
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
ABSTRACT:
Binding data are presented for the interaction with brewer's yeast tRNA(Phe) of a new structural family of ligands, symmetrical 'bis-benzimidazoles. In addition specific perturbations in chemical shifts were detected by 1-dimensional NMR spectroscopy at 400 MHz for some imino and aromatic methyl protons of tRNA(Phe) when the tRNA was titrated with distamycin. Competitive displacement of the benzimidazole by added distamycin was followed fluorescence spectroscopy.

L6 ANSWER 5 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 1998:81632 CAPLUS Full-text
DOCUMENT NUMBER: 128:240837
TITLE: Stereochemical Control of the DNA Binding Affinity, Sequence Specificity, and Orientation Preference of Chiral Hairpin Polyamides in the Minor Groove
AUTHOR(S): Herman, David M.; Baird, Eldon E.; Dervan, Peter B.
CORPORATE SOURCE: Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, CA, 91125, USA
SOURCE: Journal of the American Chemical Society (1998), 120(7), 1382-1391
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Three-ring polyamides containing pyrrole (Py) and imidazole (Im) amino acids covalently coupled by γ-aminobutyric acid (γ) form six-ring hairpins that recognize five-base-pair sequences in the ***minor*** groove of DNA. Selective chiral substitution of the "γ-turn" enhances the properties of polyamide hairpins with regard to DNA affinity and sequence specificity. ***Polyamides*** of core sequence composition ImPyPy-γ-PyPyPy which differ by selective stereochem. substitution of the prochiral α-position in the γ-turn were prepared. The DNA binding properties of two enantiomeric polyamides were analyzed by footprinting and affinity cleavage on a DNA fragment containing two match sites (5'-TGTTA-3' and 5'-ACATT-3') and one 5'-TGTCA-3' mismatch site. Quant. footprint titrns. demonstrate that replacement of γ-aminobutyric acid by (R)-2,4-diaminobutyric acid enhances DNA binding affinity for the 5'-TGTTA-3' match site 13-fold (Ka = 3.8+109 M-1). The enhanced affinity is achieved without a compromise in sequence selectivity, which in fact increases and is found to be 100-fold higher relative to binding at a single base pair mismatch sequence, 5'-TGTCA-3'. An (S)-2,4-diaminobutyric acid linked hairpin binds with 170-fold reduced affinity relative to the R-enantiomer and only 5-fold sequence specificity vs. a 5'-ACATT-3' reversed orientation site. These effects are modulated by acetylation of the chiral amine substituents. This study identifies structural elements which should facilitate the design of new hairpin polyamides with improved DNA binding affinity, sequence specificity, and orientational selectivity.

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 1998:343986 CAPLUS Full-text
DOCUMENT NUMBER: 129:119196
TITLE: A comparison of H-pin and hairpin polyamide motifs for the recognition of the minor groove of DNA
AUTHOR(S): Greenberg, William A.; Baird, Eldon E.; Dervan, Peter B.
CORPORATE SOURCE: Arnold and Mabel Beckman Lab. Chem. Synthesis, California Inst. Technol., Pasadena, CA, 91101, USA
SOURCE: Chemistry--A European Journal (1998), 4(5), 796-805
CODEN: CEUJED; ISSN: 0947-6539
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
In order to compare strategies for covalent linkage of pyrrole-imidazole (Py-Im) polyamide subunits, equilibrium association consts. (Ka) were determined for a series of polyamides coupled either C-N with a γ-aminobutyric acid linker (hairpin motif) or linked across a central Py/Py pair through a tetramethylene spacer (H-pin motif). Compared to the well-characterized hairpin motif, the H-pin motif represents a unique and relatively unexplored approach for increasing the affinity and the specificity of 2:1 polyamide-DNA complexes. Three H-pin ***polyamides*** containing 6 or 10 aromatic amino acid residues were synthesized by solid-phase methods using a Boc-protected bispyrrole monomer combined with bi-directional synthesis. The DNA-binding properties of 6-ring and 10-ring H-pin polyamides were analyzed by quant. DNase I footprint titration on a DNA fragment containing 5 or 7 base ***pair*** match and mismatch sequences, resp. The homodimeric H-Pin (ImPyPy-β-Dp)2C4 binds to the 7 base pair match sequence 5'-TGTCA-3' with Ka = 9.3 + 106M-1 and 9.4-fold specificity relative to the single base mismatch sequence 5'-TGTTA-3' (Ka = 9.9 + 105M-1). The heterodimeric H-Pin (ImPyPy-β-Dp)C4(AcPyPyPy-β-Dp) binds a 5'-TGTTA-3' match sequence with Ka = 2.0 + 106M-1 and 3.5-fold specificity vs. the single base mismatch sequence 5'-TGTCA-3' (Ka = 5.7 + 105M-1). The 10-ring H-pin (ImPyPyPyPy-β-Dp)2C4 ***binds*** to the 7 base pair match sequence 5'-TGTAACA-3' with Ka = 4.4 + 108M-1 and 28-fold specificity vs. the single base pair mismatch sequence 5'-TGGAACA-3' (Ka = 1.6 + 107M-1). H-pin polyamides bind with 4- to 180-fold enhanced affinity and 2- to 10-fold enhanced specificity relative to unlinked analogs, but with 25- to 150-fold reduced affinity and approx. 1- to 20-fold reduced specificity compared to the corresponding hairpin polyamides. These results indicate that H-pin polyamides represent a viable motif for the recognition of predetd. sequences in the DNA ***minor*** ***groove*** ; however, DNA-binding properties appear inferior to the corresponding hairpins.

REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 5
ACCESSION NUMBER: 1998:622930 CAPLUS Full-text
DOCUMENT NUMBER: 129:326670
TITLE: An analysis of a class of DNA sequence reading molecules
AUTHOR(S): Walker, Wynn L.; Goodsell, David S.; Landaw, Elliot M.
CORPORATE SOURCE: Department of Biomathematics, School of Medicine, University of California, Los Angeles, Los Angeles, CA, 90024, USA
SOURCE: Journal of Computational Biology (1998), 5(3), 571-583
CODEN: JCOBEM; ISSN: 1066-5277
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Linked polyamides are a class of designed mols. that bind in the minor groove of double stranded DNA in a partially sequence-specific manner but have limited sequence discriminatory abilities. This suggests a need for design alternatives to create mols. with enhanced sequence specificity. In this report we present formal proofs of the theor. limits of the DNA sequence specificity of hypothetical sequence reading mols. as a function of their base recognition properties and sequence content and length of their target sequence. We prove that mols.

containing nonspecific readers at critical positions within the mol. may have enhanced sequence specificity over mols. composed entirely of base specific reading elements. We also determine optimal patterns of base recognition for mols. in order to optimize their target sequence specificity. We also examine the effect of the length of a polyamide (i.e., the number of base ***pairs*** it binds) on its sequence discriminatory ability and determine necessary concentration dependent constraints on the binding free energies in order for longer polyamides to have greater sequence specificity than shorter ones. We show that unless the discriminatory ability of a ring for its preferred base is very strong, longer polyamides do not necessarily have greater sequence specificity over shorter ones when compared at the same molar concentration

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 8 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:682930 CAPLUS Full-text
DOCUMENT NUMBER: 130:34606
TITLE: Binding site of spermine at poly[d(A-T)2] and poly[d(G-C)2]
AUTHOR(S): Yun, Byeong Hwa; Jeon, Sun Hee; Song, Young-Dae; Cho, Tae-Sub; Kim, Seog K.
CORPORATE SOURCE: Dep. of Chemistry, College of Science, Yeungnam University, Kyoungbuk, 712-749, S. Korea
SOURCE: Journal of the Korean Chemical Society (1998), 42(5), 506-511
CODEN: JKCSEZ; ISSN: 1017-2548
PUBLISHER: Korean Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: Korean
ABSTRACT:
When the spermine, which is one of the polyamines containing cation in vivo, binds to DNA, it can increase the stability of ***DNA.*** At the same time, it can cause B-form to Z-form transformation of ***DNA.*** However, because we cannot determine the binding geometry of the spermine to DNA by using spectroscopic methods, nobody can show the accurate binding mechanism of a DNA-spermine complex. Thus, we used DAPI, which binding geometry was well known, as a spectroscopic probe of spermine. As the result of base selective ***binding*** geometry of spermine to synthetic DNA, when the concentration of spermine gets higher, it increases the hydrophobic environment of DAPI which bound to the minor groove of adenine-thymine ***base*** pair. Simultaneously, spermine seems to bridge the backbones around the minor groove of poly[d(A-T)2], so that the intensity of fluorescence spectrum of DAPI increased. In guanine-cytosine ***base*** pair, poly[d(G-C)2], we can suppose that spermine ***bind*** to the major groove of DNA, shoving out the DAPI which is partially intercalated between the base pocket across the major groove. In both cases, spermine does not show the base selectivity to DNA.

L6 ANSWER 9 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 6
ACCESSION NUMBER: 1998:103551 CAPLUS Full-text
DOCUMENT NUMBER: 128:291575
TITLE: Recognition of the four Watson-Crick base pairs in the DNA minor groove by synthetic ligands
AUTHOR(S): White, Sarah; Szewczyk, Jason W.; Turner, James M.; Baird, Eldon E.; Dervan, Peter B.
CORPORATE SOURCE: Div. Chem. and Chem. Eng. and Beckman Inst., California Inst. Technol., Pasadena, CA, 91125, USA
SOURCE: Nature (London) (1998), 391(6666), 468-471
CODEN: NATUAS; ISSN: 0028-0836
PUBLISHER: Macmillan Magazines
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
The design of synthetic ligands that read the information stored in the ***DNA*** double helix has been a long-standing goal at the interface of chemical and biol. Cell-permeable small mols. that target predetd. DNA sequences offer a potential approach for the regulation of gene expression. Oligodeoxynucleotides that recognize the major groove of double-helical DNA via triple-helix formation bind to a broad range of sequences with high affinity and specificity. Although oligonucleotides and their analogs have been shown to interfere with gene expression, the triple-helix approach is limited to recognition of purines and suffers from poor cellular uptake. The subsequent development of pairing rules for minor-groove binding polyamides containing pyrrole (Py) and imidazole (Im) amino acids offers a second code to control sequence specificity. An Im/Py pair distinguishes G.gtorsim.C from C.gtorsim.G and both of these from A·T/T·A base ***pairs.*** A Py/Py pair specifies A,T from G,C but does not distinguish A·T from T·A. To break this degeneracy, we have added a new aromatic amino acid, 3-hydroxypyrrole (Hp), to the repertoire to test for pairings that discriminate A·T from T.gtorsim.a. We find that replacement of a single hydrogen atom with a hydroxy group in a Hp/Py pairing regulates affinity and specificity by an order of magnitude. By incorporation of this third amino acid, hydroxypyrrole-imidazole-pyrrole polyamides form four ring-pairings (Im/Py, Py/Im, Hp/Py and Py/Hp) which distinguish all four Watson-Crick base pairs in the minor ***groove*** of DNA.

L6 ANSWER 10 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:665135 CAPLUS Full-text
DOCUMENT NUMBER: 130:32585
TITLE: Progress in the design of DNA sequence-specific lexitropsins
AUTHOR(S): Walker, Wynn L.; Kopka, Mary L.; Goodsell, David S.
CORPORATE SOURCE: Department of Biomathematics, University of California at Los Angeles, Los Angeles, CA, 90095, USA
SOURCE: Biopolymers (1998), Volume Date 1997, 44(4), 323-334
CODEN: BIPMAA; ISSN: 0006-3525
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
ABSTRACT:
A review with 44 refs. Sequence-specific polyamides that ***bind*** in the minor groove of DNA are attractive candidates for antibiotics, cancer chemotherapeutics, and transcriptional antagonists. This paper reviews the progress of structure-based design of minor-groove-binding ***polyamides*** , from the first structure of netropsin with DNA, to the effective linked polyamides currently under study. A theory of polyamide specificity is also reviewed, introducing methods to determine the optimal strategies for targeting a given DNA sequence within a genome of competing sequences.

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 11 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 7
ACCESSION NUMBER: 1998:541606 CAPLUS Full-text
DOCUMENT NUMBER: 129:254403
TITLE: Highly potent synthetic polyamides, bisdistamycins, and lexitropsins as inhibitors of human immunodeficiency virus type 1 integrase
AUTHOR(S): Neamati, Nouri; Mazumder, Abhijit; Sunder, Sanjay; Owen, Joshua M.; Tandon, Manju; Lown, J. William; Pommier, Yves
CORPORATE SOURCE: Laboratory of Molecular Pharmacology, Division of Basic Sciences, National Cancer Institute, Bethesda, MD, 20892, USA
SOURCE: Molecular Pharmacology (1998), 54(2), 280-290
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Alignment of the available human immunodeficiency virus type 1 (HIV-1) viral ***DNA*** termini [U5 and U3 long terminal repeats (LTRs)] shows a high degree of conservation and the presence of a stretch of five or six consecutive adenine and thymine (AT) sequences .apprx. 10 nucleotides away from each LTR end. A series of AT-selective minor-groove binders , including distamycin and bisdistamycins, bisnetropsins, novel lexitropsins, and the classic monomeric DNA binders Hoechst 33258, 4'-diamino-2-phenylindole, pentamidine, berenil, spermine, and spermidine, were tested for their inhibitory activities against HIV-1 integrase (IN). Although netropsin, distamycin, and all other monomeric DNA ***binders*** showed weak activities in the range of 50-200 μM, some of the polyamides, bisdistamycins, and lexitropsins were remarkably active at nanomolar concns. Bisdistamycins were 200 times less potent when the conserved AAAAT stretch present in the U5 LTR was replaced with GGGGG, consistent with the preferred binding of these drugs to AT sequences. DNase I footprinting of the U5 LTR further demonstrated the selectivity of these bisdistamycins for the conserved AT sequence. The tested compds. were more potent in Mg+2 than in Mn+2 and inhibited IN50-212 deletion mutant in disintegration assays and the formation of IN/DNA complexes. The lexitropsins also were active against HIV-2 IN. Some of the synthetic polyamides exhibited significant antiviral activity. Taken together, these data suggest that selective targeting of the U5 and U3 ends of the HIV-1 LTRs can inhibit IN function. Polyamides might represent new leads for the development of antiviral agents against acquired immune deficiency syndrome.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 12 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:523083 CAPLUS Full-text
DOCUMENT NUMBER: 129:271962
TITLE: DNA sequence recognition in the minor groove by polyamides, using a GC-specific reading element: a perspective from crystallography
AUTHOR(S): Kopka, Mary L.; Han, Gye Won; Goodsell, David S.; Chiu, Thang Kien; Walker, Wynn L.; Lown, J. W.; Dickerson, Richard E.
CORPORATE SOURCE: Molecular Biology Institute and Department of Biomathematics, University of California at Los Angeles, Los Angeles, CA, 90095, USA
SOURCE: Structure, Motion, Interaction and Expression of Biological Macromolecules, Proceedings of the Conversation in the Discipline Biomolecular Stereodynamics, 10th, Albany, June 17-21, 1997 (1998), Meeting Date 1997, Volume 1, 177-194. Editor(s): Sarma, Ramaswamy H.; Sarma, Mukti H. Adenine Press: Schenectady, N. Y.
CODEN: 66NGAV
DOCUMENT TYPE: Conference
LANGUAGE: English
ABSTRACT:
The 2:1 binding mode of polyamide lexitropsins containing imidazole (Im) and pyrrole (Py) rings produces a side-by-side binding motif in which a ring from each drug mol. sits at a given base ***pair.*** Side-by-side binding causes little perturbation to the ***DNA*** helix. A narrow groove of AT base pairs can widen to accept two side-by-side polyamides, whereas an already wide groove of mixed sequence needs only slight adjustment to bind two drug mols. alongside one another. Ribbons of water mols. continue to line the groove along each wall of a wide groove in regions where drugs are not bound. An individual drug ring is stacked in a "sandwich" between an amide of the neighboring drug mol. and an O4' sugar atom of the DNA backbone. Side-by-side imidazole and pyrrole rings can differentiate GC from CG ***base*** pairs because the imidazole prefers to sit on the guanine side and make a hydrogen bond to its 2-amino group: Im,Py favors GC, whereas Py,Im prefers CG. Side-by-side Py,Py and Im,Im rings select AT and GC ***base*** pairs, resp., without regard to end-for-end base ***pair*** orientation. The x-ray crystal structure containing Im,Im pairs shows that the specificity of Im for guanosine is a combination of optimum bond distances and sp2 hybridization geometry about the guanine N2 atom. It is proposed that a bulky thiazole (Th) ring may be a potential discriminator for adenine, as imidazole is for guanine. If so, the Th,Py would recognize AT, and Py,Th would recognize TA, thus permitting end-for-end discrimination in AT ***base*** pairs. This would open the door to complete sequence readout in the minor groove of DNA.

REFERENCE COUNT: 75 THERE ARE 75 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 13 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:139659 CAPLUS Full-text
TITLE: Regulation of gene expression by small molecules.
AUTHOR(S): Dervan, Peter B.
CORPORATE SOURCE: Division Chemistry and Chemical Engineering, California Institute Technology, Pasadena, CA, 91125, USA
SOURCE: Book of Abstracts, 215th ACS National Meeting, Dallas, March 29-April 2 (1998), ORGN-141. American Chemical Society: Washington, D. C.
CODEN: 65QTAA
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
ABSTRACT:
Small mols. that specifically bind at subnanomolar concns. to any predetd. DNA sequence in the human genome would be useful tools in biol. and potentially in human medicine. Pairing rules have been developed to control rationally the DNA sequence specificity of minor-***groove*** -binding polyamides containing N-methylimidazole and N-methylpyrrole amino acids. An imidazole ring paired antiparallel with a pyrrole recognizes a G•C base pair, whereas a pyrrole-imidazole combination targets a C•G base pair. A pyrrole/pyrrole pair is degenerate for A•T or T•A base ***pairs.*** Using a simple mol. shape and a two-letter aromatic amino-acid code, eight-ring pyrrole-imidazole polyamides achieve affinities and specificities comparable to DNA-binding proteins and, in addition, have the potential to be general for any desired DNA sequence. This non-biol. approach to DNA recognition could provide an underpinning for the design of cell-permeable mols. for the control of gene-specific regulation in vivo.

L6 ANSWER 14 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 8
ACCESSION NUMBER: 1998:241584 CAPLUS Full-text
DOCUMENT NUMBER: 129:24703
TITLE: Inhibition of major-groove-binding proteins by pyrrole-imidazole polyamides with an Arg-Pro-Arg positive patch
AUTHOR(S): Bremer, Ryan E.; Baird, Eldon E.; Dervan, Peter B.
CORPORATE SOURCE: Arnold and Mabel Beckman Laboratories of Chemical Synthesis, California Institute of Technology, Pasadena, CA, 91 125, USA
SOURCE: Chemistry & Biology (1998), 5(3), 119-133
CODEN: CBOLE2; ISSN: 1074-5521
PUBLISHER: Current Biology Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Gene-specific targeting of any protein-DNA complex by small mols. is a challenging goal at the interface of chemical and biol. Polyamides containing N-methylimidazole and N-methylpyrrole amino acids are synthetic ligands that have an affinity and specificity for DNA comparable to many naturally occurring DNA-binding proteins. It has been shown that an eight-ring hairpin polyamide targeted to a specific ***minor*** -groove contact within a transcription factor ***binding*** site can inhibit protein-DNA ***binding*** and gene transcription. Polyamides and certain ***major*** -groove-binding proteins have been found to co-occupy the DNA helix, however. To expand the number of genes that can be targeted by pyrrole/imidazole polyamides, we set out to develop a class of polyamides that can selectively inhibit ***major*** -groove-binding proteins. An eight-ring hairpin polyamide conjugated to a carboxy-terminal Arg-Pro-Arg tripeptide was designed to deliver a pos. residue to the DNA backbone and interfere with protein-phosphate contacts. Gel mobility shift anal. demonstrated that a polyamide hairpin-Arg-Pro-Arg binding in the minor groove selectively inhibits ***binding*** of the transcription factor GCN4 (222-281) in the adjacent ***major*** groove. Substitution within the Arg-Pro-Arg revealed that each residue was required for optimal GCN4 inhibition. A pyrrole-imidazole polyamide that binds to a predetd. site in the DNA minor groove and delivers a pos. patch to the DNA backbone can selectively inhibit a DNA -binding protein that recognizes the adjacent major ***groove.*** A subtle alteration of the DNA microenvironment targeted to a precise location within a specific DNA sequence could achieve both gene-specific and protein-specific targeting.

REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 15 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 9
ACCESSION NUMBER: 1998:88936 CAPLUS Full-text
DOCUMENT NUMBER: 128:254196
TITLE: Structural basis for G•C recognition in the DNA minor groove
AUTHOR(S): Kielkopf, Clara L.; Baird, Eldon E.; Dervan, Peter B.; Rees, Douglas C.
CORPORATE SOURCE: Division Biology, California Institute Technology, Pasadena, CA, 91125, USA
SOURCE: Nature Structural Biology (1998), 5(2), 104-109
CODEN: NSBIEW; ISSN: 1072-8368
PUBLISHER: Nature America
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Small mols. that target specific DNA sequences offer a potentially general approach for the regulation of gene expression. Pyrrole-imidazole ***polyamides*** represent the only class of synthetic small mols. that can ***bind*** predetd. DNA sequences with affinities and specificities comparable to DNA binding proteins. Antiparallel side-by-side pairings of two aromatic amino acids, imidazole (Im) and pyrrole (Py), distinguish G•C form C•G, and both from A•T/T•A ***base*** pairs. A high resolution x-ray crystal structure of a four-ring pyrrole-imidazole polyamide specifically bound as a dimer to a six-base pair predetd. DNA site reveals a structural framework of hydrogen bonds and interactions with the walls of the ***minor*** groove that underlies the pairing rules for DNA recognition.

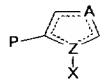
REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 16 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:1336 CAPLUS Full-text
DOCUMENT NUMBER: 128:85623
TITLE: Triheterocyclic peptides capable of binding the minor and major grooves of DNA
INVENTOR(S): Bruice, Thomas C.; Browne, Kenneth A.; He, Gong-Xin

PATENT ASSIGNEE(S): University of California, USA
SOURCE: U.S., 66 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5698674	A	19971216	US 1994-226934	19940413

PRIORITY APPLN. INFO.: US 1994-226934 19940413
OTHER SOURCE(S): MARPAT 128:85623
GRAPHIC IMAGE:



I

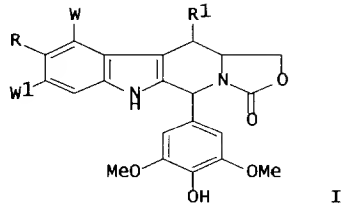
II

ABSTRACT:
The present invention provides a tripyrrole peptide having first, second, and third pyrrole rings, said peptide binding DNA thereby prohibiting the binding of DNA with an enzyme that regulates DNA expression and/or replication. The tripyrrole peptide has a polyamine group attached to the nitrogen atom of the second pyrrole and binds to the minor groove of ***DNA*** with an equilibrium constant of >109M-1 and is incapable of alkylating the enzyme of DNA. Also provided is a triheterocyclic peptide having first, second, and third 5-member heterocyclic moieties having the following formula CR3CONH-Q-CONH-Q-CONH-Q-CONH-(CR3)s-B (Q = I or II; ≥1 of A and Z is other than C; A = C, N, O, S; B = N(CR3)n or C(NH2)2 ; n = 2-10; P = H, lower alkyl, halogen; R = H, lower alkyl group; s = 1-10; X = CR3, (CR2)n-NRY, (CR2)n-CR2Y; Y = polyamine group; Z = C, N; ≥1 X is other than CR3). The polyamine group may be cyclen; 1,4,7-triazacyclononane; tris(3-aminopropyl)amine; 1,5,9-triazacyclododecane and other metal-***binding*** moieties. The synthesis of two tren-microgonotropens as well as their interaction with DNA was described.

L6 ANSWER 17 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:311166 CAPLUS Full-text
DOCUMENT NUMBER: 126:343431
TITLE: Preparation of azatoxins as topoisomerase II inhibitors
INVENTOR(S): Pommier, Yves; MacDonald, Timothy L.; Madalengoitia, Jose S.
PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA
SOURCE: U.S., 19 pp., Cont.-in-part of U.S. Ser. No. 868,408, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5622960	A	19970422	US 1992-965922	19921023
CA 2147608	AA	19940511	CA 1993-2147608	19931014
WO 9410175	A1	19940511	WO 1993-US9629	19931014
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9453254	A1	19940524	AU 1994-53254	19931014
AU 676511	B2	19970313		
EP 665846	A1	19950809	EP 1993-923324	19931014
EP 665846	B1	19980729		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
AT 169022	E	19980815	AT 1993-923324	19931014
US 5606060	A	19970225	US 1995-460742	19950602
US 5747520	A	19980505	US 1995-460754	19950602

PRIORITY APPLN. INFO.: US 1992-868408 B2 19920414
US 1992-965922 A 19921023
WO 1993-US9629 W 19931014
OTHER SOURCE(S): MARPAT 126:343431
GRAPHIC IMAGE:



I

ABSTRACT:
Azatoxin and derivs. thereof are illustrative of a new class of antitumor drugs that are topoisomerase II (top 2) inhibitors. The pharmacophore ***inhibits*** the catalytic activity of the purified enzyme but does not unwind relaxed or supercoiled DNA. It is nonintercalative and has at least two domains: a quasi-planar polycyclic ring system, which may ***bind*** between DNA base pairs, and a pendant substituent thought to interact with the enzyme, with the DNA grooves or with both. In SV40 and c-myc DNA, azatoxin induces numerous double-strand breaks according to a cleavage pattern which differs from those of known top 2 inhibitors. Azatoxin also is a potent ***inhibitor*** of tubulin polymerization. Azatoxins I [R = F, Cl, Br, CN, OH, NH2, H; R1 = arylamino, substituted alkoxy, alkylamino, protected sugar derivative; W, W1 = H, F] were prepared. Thus, tryptophanol was cyclized to the oxazolidone and treated with syringaldehyde dimethylacetal to give (5R,11aS)-I [R, R1, W, W1 = H] which is a top 2 inhibitor.

L6 ANSWER 18 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 10
ACCESSION NUMBER: 1997:800768 CAPLUS Full-text
DOCUMENT NUMBER: 128:164237
TITLE: Cloning, expression, and properties of the regulatory subunit of bovine pyruvate dehydrogenase phosphatase
AUTHOR(S): Lawson, Janet E.; Park, Seung Hee; Mattison, Angela R.; Yan, Jiangong; Reed, Lester J.
CORPORATE SOURCE: Biochemical Institute and Department of Chemistry and Biochemistry, The University of Texas at Austin, Austin, TX, 78712, USA
SOURCE: Journal of Biological Chemistry (1997), 272(50), 31625-31629
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
CDNA encoding the regulatory subunit of bovine mitochondrial pyruvate dehydrogenase phosphatase (PDPr) has been cloned. Overlapping cDNA fragments were generated by the polymerase chain reaction from bovine genomic DNA and from cDNA synthesized from bovine poly(A)+ RNA and total ***RNA.*** The complete cDNA (2885 base pairs) contains an open reading frame of 2634 nucleotides encoding a putative presequence of 31 amino acid residues and a mature protein of 847 residues with a calculated Mr of 95,656. This value is in agreement with the mol. mass of native PDPr (95,800±200 Da) determined by matrix-assisted laser desorption-ionization mass spectrometry. The mature form of PDPr was expressed in Escherichia coli as a maltose-binding protein fusion, and the recombinant protein was purified to near homogeneity. It exhibited properties characteristic of the native PDPr, including recognition by antibodies against native bovine PDPr, ability to decrease the sensitivity of the catalytic subunit to Mg2+, and reversal of this inhibitory effect by the polyamine spermine. A BLAST search of protein data bases revealed that PDPr is distantly related to the mitochondrial flavoprotein dimethylglycine dehydrogenase, which functions in choline degradation

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 19 OF 98 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 97:869106 SCISEARCH Full-text
THE GENUINE ARTICLE: YG273
TITLE: A novel peptide nucleic acid monomer for recognition of

thymine in triple-helix structures
AUTHOR: Eldrup A B; Dahl O; Nielsen P E (Reprint)
CORPORATE SOURCE: UNIV COPENHAGEN, PANUM INST, DEPT BIOCHEM B, BLEGDAMSVEJ 3, DK-2200 COPENHAGEN N, DENMARK (Reprint); UNIV COPENHAGEN, PANUM INST, DEPT BIOCHEM B, DK-2200 COPENHAGEN N, DENMARK; UNIV COPENHAGEN, DEPT CHEM, CTR BIOMOL RECOGNIT, DK-2100 COPENHAGEN O, DENMARK
COUNTRY OF AUTHOR: DENMARK
SOURCE: JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, (12 NOV 1997) Vol. 119, No. 45, pp. 11116-11117. Publisher: AMER CHEMICAL SOC, 1155 16TH ST, NW, WASHINGTON, DC 20036. ISSN: 0002-7863.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: PHYS; LIFE
LANGUAGE: English
REFERENCE COUNT: 26

L6 ANSWER 20 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 11
ACCESSION NUMBER: 1997:528939 CAPLUS Full-text
DOCUMENT NUMBER: 127:216523
TITLE: NMR Characterization of Hairpin Polyamide Complexes with the Minor Groove of DNA
AUTHOR(S): Lamamie de Clairac, Rafael Pelaez; Geierstanger, Bernhard H.; Mrksich, Milan; Dervan, Peter B.; Wemmer, David E.
CORPORATE SOURCE: Department of Chemistry, University of California, Berkeley, CA, 94720, USA
SOURCE: Journal of the American Chemical Society (1997), 119(34), 7909-7916 CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Polyamides containing N-methylimidazole (Im) and N-methylpyrrole (Py) amino acids can be combined in antiparallel side-by-side dimeric complexes for sequence-specific recognition in the minor groove of ***DNA.*** Covalently linking polyamide subunits has led to designed ligands with both increased affinity and specificity. Simple aliphatic amino acid linkers serve as internal guide residues for turn vs. extended ***binding*** in a head-to-tail-linked polyamide motif. ***Polyamides*** of sequence composition ImPyPy-X-PyPyPy containing linkers of incremental length (X = 3-aminopropionic acid (β), 4-aminobutyric acid (γ), or 5-aminovaleric acid (δ)) in complex with an undecamer ***DNA*** duplex containing a 5'-(A,T)G(A,T)3-3' target site were structurally characterized using NMR spectroscopy. Previous quant. DNase I footprinting studies identified γ as the highest affinity of these "turn" linkers. NMR titrns. and 2D NOESY data combined with restrained mol. modeling reveal that polyamides with β, γ, and δ linkers all may adopt a hairpin structure. Modeling supports the idea that the linkers in the β and δ complexes adopt an energetically less favorable turn geometry than the γ linker and confirms that the three-carbon γ linker is sufficient and optimal for the hairpin conformation.

L6 ANSWER 21 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 12
ACCESSION NUMBER: 1997:528757 CAPLUS Full-text
DOCUMENT NUMBER: 127:216506
TITLE: Recognition of Seven Base Pair Sequences in the Minor Groove of DNA by Ten-Ring Pyrrole-Imidazole Polyamide Hairpins
AUTHOR(S): Turner, James M.; Baird, Eldon E.; Dervan, Peter B.
CORPORATE SOURCE: Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, CA, 91125, USA
SOURCE: Journal of the American Chemical Society (1997), 119(33), 7636-7644 CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
A new upper limit of binding site size is defined for the hairpin ***polyamide*** -DNA motif. Ten-ring hairpin polyamides containing pyrrole (Py) and imidazole (Im) amino acids were designed for recognition of seven base pair (bp) sequences in the ***minor*** groove of DNA. The DNA ***binding*** properties of two polyamides, ImPyPyPyPy-γ-ImPyPyPyPy-β-Dp, and ImImPyPyPy-γ-ImPyPyPyPy-β-Dp were analyzed by footprinting and affinity cleavage on a DNA fragment containing the resp. match sites 5'-TGTAACA-3' and 5'-TGGAACA-3'. Quant. footprint titrns. demonstrate that ImPyPyPyPy-γ-ImPyPyPyPy-β-Dp binds the 7-bp match sequence 5'-TGTAACA-3' with an equilibrium association constant (Ka) of Ka = 1.2 + 1010 M-1 and 18-fold specificity vs. the single base ***pair*** mismatch sequence 5'-TGGAACA-3'. ImImPyPyPy-γ-ImPyPyPyPy-β-Dp differs from ImPyPyPyPy-γ-ImPyPyPyPy-β-Dp by a single amino acid substitution and binds its match 5'-TGGAACA-3' site with Ka = 3.6 + 109 M-1 and 300-fold specificity vs. its corresponding single ***base*** pair mismatch sequence 5'-TGTAACA-3'. Ten-ring hairpin ***polyamides*** have binding affinities similar to those of eight-ring hairpin polyamides. These results indicate that the affinity of hairpin binding ceases to increase as the length of the ***polyamide*** subunits increases beyond four rings, analogous to the behavior of unlinked subunits. Therefore, recognition of seven base ***pairs*** by a ten-ring hairpin polyamide most likely represents an upper limit to the effective targetable site size of the hairpin ***polyamide*** -DNA motif.

L6 ANSWER 22 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 13
ACCESSION NUMBER: 1997:500223 CAPLUS Full-text
DOCUMENT NUMBER: 127:158066
TITLE: Discrimination of 5'-GGGG-3', 5'-GCGC-3', and 5'-GGCC-3' sequences in the minor groove of DNA by eight-ring hairpin polyamides
AUTHOR(S): Swalley, Susanne E.; Baird, Eldon E.; Dervan, Peter B.
CORPORATE SOURCE: Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, CA, 91125, USA
SOURCE: Journal of the American Chemical Society (1997), 119(30), 6953-6961 CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Eight-ring hairpin polyamides which differ only by the linear arrangement of pyrrole (Py) and imidazole (Im) amino acids were designed for recognition of 6-bp pair DNA sequences containing 4 contiguous G,C ***base*** pairs. The resp. DNA binding properties of 3 polyamides, ImImPyPy-γ-ImImPyPy-β-Dp, ImPyImPy-γ-ImPyImPy-β-Dp, and ImImImIm-γ-PyPyPyPy-β-Dp, were analyzed by footprinting and affinity cleavage on a DNA fragment containing the resp. match sites 5'-TGGCCA-3', 5'-TGCGCA-3', and 5'-TGGGGA-3'. Quant. footprint titrns. demonstrate that ImImPyPy-γ-ImImPyPy-β-Dp ***binds*** the designed match site 5'-TGGCCA-3' with an equilibrium association constant of Ka = 1 + 1010 M-1 and >250-fold specificity vs. the mismatch sequences, 5'-TGCGCA-3' and 5'-TGGGGA-3'. The polyamides ImPyImPy-γ-ImPyImPy-β-Dp and ImImImIm-γ-PyPyPyPy-β-Dp recognize their resp. 5'-TGCGCA-3' and 5'-TGGGGA-3' match sites with reduced affinity relative to ImImPyPy-γ-ImImPyPy-β-Dp, but again with high specificity with regard to mismatch sites. These results expand the ***DNA*** sequence repertoire targeted by pyrrole-imidazole ***polyamides*** and identify sequence composition effects which will guide further second-generation polyamide design for DNA recognition.

L6 ANSWER 23 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 14
ACCESSION NUMBER: 1997:356731 CAPLUS Full-text
DOCUMENT NUMBER: 127:77460
TITLE: Estimation of the DNA sequence discriminatory ability of hairpin-linked lexitropsins
AUTHOR(S): Walker, Wynn L.; Landaw, Elliot M.; Dickerson, Richard E.; Goodsell, David S.
CORPORATE SOURCE: Dep. Biomathematics and the Mol. Biol. Inst., Univ. California, Los angeles, CA, 90024, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1997), 94(11), 5634-5639 CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Three- and four-ring polyamides containing N-methylimidazole and N-methylpyrrole, and their hairpin-linked derivs., bind side-by-side in the minor groove of DNA in a sequence-specific manner. The sequences recognized by side-by-side mols. are dependent on the pairing of the polyamide rings to the bases. This study reports a math. model for estimating the free energies of binding for γ-aminobutyric acid-linked polyamides to 5- and 6-bp ***DNA*** sequences. The model parameters are calibrated by a least-squares fit to 35 exptl. binding consts. The model performs well in cross-validation expts. and the parameters are consistent with previously proposed empirical rules of polyamide-DNA binding

. The model was applied to the design of targeted polyamides, evaluating the ability of the proposed polyamides to bind to a DNA sequence of interest while minimizing binding to the remaining DNA sequences.

L6 ANSWER 24 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 15
ACCESSION NUMBER: 1997:290189 CAPLUS Full-text
DOCUMENT NUMBER: 126:340138
TITLE: Monte Carlo Simulation Study of DNA Polyelectrolyte Properties in the Presence of Multivalent Polyamine Ions
AUTHOR(S): Lyubartsev, Alexander P.; Nordenskioeld, Lars
CORPORATE SOURCE: Division of Physical Chemistry Arrhenius Laboratory, Stockholm University, Stockholm, S 106 91, Swed.
SOURCE: Journal of Physical Chemistry B (1997), 101(21), 4335-4342
CODEN: JPCBFK; ISSN: 1089-5647
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Properties of ionic distributions of mixts. of atomic (Na+, Mg2+, Cl-) and mol. (spermidine3+) ions in the vicinity of DNA have been studied by the Monte Carlo simulation method, within the frame of a continuum dielec. approach. Several models differing by the level of approxns. have been considered and compared. In one of these models the DNA phosphate charge distribution is described by point charges in a double helical array corresponding to B-DNA, thus in an idealized way incorporating the ***major*** and minor groove structure. Ion distribution profiles, ion binding properties, and competition effects in the association of the different counterions to DNA have been studied. Particular attention has been paid to the importance of the discrete distribution of the three charges on the spermidine mol. model. The work has shown that the behavior of complex multivalent ions differs strongly from the properties of simple metal ions of the same valence. The competitive behavior and binding properties of the spermidine mol. modeled with distributed charges appear to be reduced from those expected for point charge (or spherical) three-valent ions, even compared to the predictions of the Poisson-Boltzmann approximation, and more likely correspond to the behavior of atomic divalent ions. The results of binding properties was found to be in qual. agreement with existing NMR diffusion studies of polyamine association to DNA.

L6 ANSWER 25 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 16
ACCESSION NUMBER: 1997:246308 CAPLUS Full-text
DOCUMENT NUMBER: 126:312222
TITLE: Targeting E2F1-DNA complexes with microgonotropen DNA binding agents
AUTHOR(S): Chiang, Shu-Yuan; Bruice, Thomas C.; Azizkhan, Jane C.; Gawron, Loretta; Beerman, Terry A.
CORPORATE SOURCE: Experimental Therapeutics Department, Roswell Park Cancer Institute, Buffalo, NY, 14263, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1997), 94(7), 2811-2816
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Microgonotropen (MGT) DNA binding drugs, which consist of an A+T-selective DNA minor groove binding tripyrrole peptide and polyamine chains attached to a central pyrrole that extend drug contact into the DNA major groove , were found to be extraordinarily effective inhibitors of E2 factor 1 (E2F1) association with its DNA promoter element (5'-TTTCGCGCCAAA). The most active of these drugs, MGT-6a, was three orders of magnitude more effective than distamycin and inhibited complexes between E2F1 and the dihydrofolate reductase promoter by 50% at 0.00085 μM. A relationship was found between the measured equilibrium consts. for binding of MGTs to the A+T region of d(GGCGA3T3GGC)/d(CCGCT3A3CCG) and their inhibition of complex formation between E2F1 and the DNA promoter element. A representative of the potent MGT inhibitors was significantly more active on inhibition of E2F1-DNA complex formation compared with disruption of a preexisting complex.

L6 ANSWER 26 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 17
ACCESSION NUMBER: 1997:749357 CAPLUS Full-text
DOCUMENT NUMBER: 128:99029
TITLE: A pyrrole-imidazole polyamide motif for recognition of eleven base pair sequences in the minor groove of DNA
AUTHOR(S): Swalley, Susanne E.; Baird, Eldon E.; Dervan, Peter B.
CORPORATE SOURCE: Arnold and Mabel Beckman Laboratories of Chemical Synthesis, California Institute of Technology, Pasadena, CA, 91101, USA
SOURCE: Chemistry--A European Journal (1997), 3(10), 1600-1607
CODEN: CEUJED; ISSN: 0947-6539
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
A new upper limit of binding site size is defined for the 2:1 overlapped polyamide: DNA motif. Eight-ring ***polyamides*** composed of four-ring subunits containing pyrrole (Py) and imidazole (Im) amino acids linked by a central β-alanine (β) spacer ("4-β-4 ligands") were designed for recognition of eleven base ***pair*** sequences as antiparallel dimer (4-β-4)2.cntdot.DNA complexes in the minor groove. The DNA ***binding*** properties of three polyamides, ImPyPyPy-β-PyPyPyPy-β-Dp, ImImPyPy-β-PyPyPyPy-β-Dp, and ImImImPy-β-PyPyPyPy-β-Dp, were analyzed by footprinting expts. on ***DNA*** fragments containing the resp. match sites 5'-AGTAATTTACT-3', 5'-AGGTATTACCT-3', and 5'-AGGGATTCCCT-3' (Dp = dimethylaminopropylamide). Quant. footprint titrns. reveal that each polyamide binds its resp. target site with subnanomolar affinity and 7-fold to over 30-fold specificity over double-base-pair mismatch sites. A 20-fold decrease in binding affinity is observed for placement of a side-by-side β-β pairing opposite G·C/C·G relative to placement opposite a A·T/T·A base pair. The use of side-by-side antiparallel β-alanine residues as an A·T/T·A-specific DNA binding element provides a new pairing rule for polyamide design. Expanding the DNA ***binding*** site size targeted by pyrrole-imidazole polyamides represents an important step in the development of cell-permeable synthetic ligands for the control of gene-specific regulation.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 27 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 18
ACCESSION NUMBER: 1997:285945 CAPLUS Full-text
DOCUMENT NUMBER: 127:30549
TITLE: Hairpin polyamides that use parallel and antiparallel side-by-side peptide motifs in binding to DNA
AUTHOR(S): Surovaya, Anna N.; Burckhardt, Gunther; Grokhovsky, Sergei L.; Birch-Hirschfeld, Eckhard; Gursky, Georgii V.; Zimmer, Christoph
CORPORATE SOURCE: Engelhardt Institute of Molecular Biology, Russian Academy of Sciences, Moscow, 117894, Russia
SOURCE: Journal of Biomolecular Structure & Dynamics (1997), 14(5), 595-606
CODEN: JBSDD6; ISSN: 0739-1102
PUBLISHER: Adenine Press
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Pt-bis-netropsin is a synthetic sequence-specific DNA-binding ligand comprising two netropsin-like fragments which are linked in a tail-to-tail manner via a cis-diammineplatinum(II) residue. The CD studies and thermodn. characterization of the DNA-binding properties exhibited by this compound reveal that it forms two types of complexes with poly[d(AT)]·poly[d(AT)] and DNA oligomers containing nucleotide sequences 5'-CC(TA)n CC-3', with n = 4, 5 and 6. The first type corresponds to the binding of Pt-bis-netropsin in the extended conformation and is characterized by the saturating ratio of one bound Pt-bis-netropsin mol. per 9 AT-***base*** pairs. The second type of the complex corresponds to the binding of Pt-bis-netropsin to DNA in the folded hairpin form. The binding approaches saturation level when one Pt-bis-netropsin mol. is bound per four or five AT-base pairs . The hairpin form of Pt-bis-netropsin complex is built on the basis of parallel side-by-side peptide motif which is inserted in the minor ***DNA*** groove. The CD spectral profiles reflecting the ***binding*** of Pt-bis-netropsin in the hairpin form are different from those observed for binding of another bis-netropsin with the sequence Lys-Gly-Py-Py-Gly-Gly-Gly-Py-Py-Dp, where Py is a N-propylpyrrole amino acid residue and Dp is a dimethylaminopropylamino residue. The hairpin form of this bis-netropsin is formed on the basis of antiparallel side-by-side peptide motif. The CD spectra obtained for complexes of this polyamide in the hairpin form with poly[d(AT)]·poly[d(AT)] exhibit pos. CD band with a peak at 325 nm, whereas the CD spectral profiles for the second complex of Pt-bis-netropsin with poly[d(AT)]·poly[d(AT)] and short DNA oligomers have two intense pos. CD bands near 290 nm and 328 nm. This reflects the fact that two bis-netropsins use different structural motifs on ***binding*** to DNA in the hairpin form.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 28 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 19
ACCESSION NUMBER: 1997:324485 CAPLUS Full-text
DOCUMENT NUMBER: 127:46509
TITLE: Design of sequence-specific DNA-binding ligands
AUTHOR(S): Nielsen, Peter E.
CORPORATE SOURCE: Cent. Biomolecular Recognition, Dep. Biochem. and Genetics Biochem. Lab. B, Panum Inst., Copenhagen, DK-2200 N, Den.
SOURCE: Chemistry--A European Journal (1997), 3(4), 505-508
CODEN: CEUJED; ISSN: 0947-6539
PUBLISHER: VCH
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
ABSTRACT:
A review with 25 refs. Double-stranded DNA can be viewed as a multifunctional, modular receptor that can be read sequence-selectively in a digital way (base pair per base pair) by a complementary, similarly modular ligand. This principle has been exploited in several approaches to design sequence-specific DNA-***binding*** ligands, such as triplex-forming oligonucleotides, peptide nucleic acids and minor groove binding ***polyamides.***

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 29 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 20
ACCESSION NUMBER: 1998:12930 CAPLUS Full-text
DOCUMENT NUMBER: 128:163538
TITLE: Importance of minor groove binding zinc fingers within the transcription factor IIIA-DNA complex
AUTHOR(S): Neely, Laura; Trauger, John W.; Baird, Eldon E.; Dervan, Peter B.; Gottesfeld, Joel M.
CORPORATE SOURCE: Department of Molecular Biology, The Scripps Research Institute, La Jolla, CA, 92037, USA
SOURCE: Journal of Molecular Biology (1997), 274(4), 439-445
CODEN: JMOBAK; ISSN: 0022-2836
PUBLISHER: Academic Press Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
The gene-specific transcription factor IIIA (TFIIIA) binds to the internal promoter element of the 5 S rRNA gene through nine zinc fingers which make specific DNA contacts. Seven of the nine TFIIIA zinc fingers participate in major groove DNA contacts while two fingers, 4 and 6, have been proposed to bind in or across the ***minor*** groove. Pyrrole-imidazole polyamides are ***minor*** groove binding ligands that recognize predetd. DNA sequences with affinity and specificity comparable to natural DNA-binding proteins. We have examined the ***DNA*** binding activity of nine finger TFIIIA and shorter recombinant analogs in the presence of polyamides that bind six base-pair sequences (Kd = 0.03 to 1.7 nM) in the ***minor*** groove of the binding site for zinc finger 4. DNase I footprint titrns. demonstrate that the polyamides and a recombinant protein containing the three amino-terminal zinc fingers of TFIIIA (zf1-3) cooccupy the TFIIIA binding site, in agreement with the known location of zf1-3 in the major groove. In contrast, the ***polyamides*** block the specific interaction of TFIIIA or zf1-4 with the 5 S RNA gene, supporting a model for minor groove occupancy by zinc finger 4. Minor groove binding ***polyamides*** targeted to specific DNA sequences may provide a novel chemical approach to probing multidomain protein-DNA interactions.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 30 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 21
ACCESSION NUMBER: 1997:341254 CAPLUS Full-text
DOCUMENT NUMBER: 127:29674
TITLE: Recognition of DNA sequence and DNA bending. Molecular design for artificial repressor
AUTHOR(S): Sugiura, Yukio; Nagaoka, Makoto
CORPORATE SOURCE: Inst. Chem. Res., Kyoto Univ., Uji, 611, Japan
SOURCE: Yuki Gosei Kagaku Kyokaishi (1997), 55(5), 384-392
CODEN: YGKKAE; ISSN: 0037-9980
PUBLISHER: Yuki Gosei Kagaku Kyokai
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
ABSTRACT:
A review with 32 refs. DNA recognition is a very important phenomenon in biol. and chemical, and the mol. basis of the sequence-specific ***DNA*** binding is the subject of investigations aimed at the rational design of mols. with specific biol. activities. Minor-***groove*** -binding polyamides containing N-methylimidazole and N-methylpyrrole amino acids achieve affinities and specificities comparable to DNA binding proteins. The synthetic oligosaccharide moiety of the antibiotic calicheamicin and the head-to-head dimer of this oligosaccharide bind to the minor groove of ***DNA*** in a sequence-selective manner preferring distinct target sequences. Zinc-finger libraries with different DNA-binding specificities based on a one-finger-three-nucleotide code have been developed successfully. On the other hand, DNA bending is also important regulators of biol. process. Sequence-specific DNA bending ligands are designed to bind 2 noncontiguous sites in the major ***groove*** and induce a bent in the DNA. Mols. that specifically ***bind*** and bent any predetd. DNA sequence in the human genome would be useful tools in mol. biol. and potentially in human medicine.

L6 ANSWER 31 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 22
ACCESSION NUMBER: 1997:339542 CAPLUS Full-text
DOCUMENT NUMBER: 127:78163
TITLE: Ru(II)-polyaminopolycarboxylate complexes for improved DNA probes
AUTHOR(S): Shepherd, Rex E.; Chen, Ya; Zhang, Songsheng; Lin, Fu-Tyan; Kortes, Richard A.
CORPORATE SOURCE: Department Chemistry, University Pittsburgh, Pittsburgh, PA, 15260, USA
SOURCE: Advances in Chemistry Series (1997), 253(Electron Transfer Reactions), 367-397
CODEN: ADCSAJ; ISSN: 0065-2393
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
The potential use of ruII polyaminopolycarboxylates (RuII-pacs) to ***bind*** at the C5-C6 bonds of pyrimidine nucleobases of DNA and, as a binuclear derivative, to span the major groove of ***DNA*** is discussed. A complex that illustrates this potential chemotherapeutic use is presented in studies of [Ru2(rrha)(DMU)2]2- (ttha6- = triethylenetetraminehexacetate; DMU = 1,3-dimethyluracil). Factors in promoting η2 attachments that will dearomatize diazines are examined in studies of [RuII(hedta)(H2O)]- in coordination with pyrimidines (pyrimidine, 4-methylpyrimidine, and 4,6-dimethylpyrimidine) and pyridazine (pyd). Rapid coordination of pyrimidines and pyridazine occurs at the N1 position. A further migration to η2(1,2), η2(1,6), and η2(5,6) locations occurs slowly for pyrimidines. The η2 attachments are described by 1H NMR assignments. Coordination at N1 of pyd is followed by an internal nucleophilic substitution of the enhanced nitrogen base at N2. The asym. coordinated bidentate [Ru(hedta)(pyd)]- complex readily forms the bis derivative by disrupting the strained RuII-pyd bonding. Structural factors that optimize RuII-pac coordination for olefins or pyrimidine nucleobases are studied with [S,S-Ru(Me2edda)(H2O)2]. The best RuII-pac for η2 DNA coordination would have a metallo headgroup that utilizes the coordination of the asym. ligand N,N-ethylenediaminediacetate for the RuII center.

L6 ANSWER 32 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 23
ACCESSION NUMBER: 1997:390973 CAPLUS Full-text
DOCUMENT NUMBER: 127:118629
TITLE: Targeting the minor groove of DNA
AUTHOR(S): Wemmer, David E.; Dervan, Peter B.
CORPORATE SOURCE: Department Chemistry, MC-1460, University California, Berkeley, CA, 94620-1460, USA
SOURCE: Current Opinion in Structural Biology (1997), 7(3), 355-361
CODEN: COSBEF; ISSN: 0959-440X
PUBLISHER: Current Biology
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
ABSTRACT:
A review with 47 refs. Small mols. that specifically bind with high affinity to any predetd. DNA sequence in the human genome will be useful tools in mol. biol. and, potentially, in human medicine. Pairing rules have been developed to control rationally the sequence specificity of ***minor*** groove binding polyamides containing N-methylimidazole and N-methylpyrrole amino acids. Using simple mol. shapes and a two-letter aromatic amino acid code, pyrrole-imidazole polyamides achieve affinities and specificities comparable to DNA-***binding*** proteins.

L6 ANSWER 33 OF 98 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN DUPLICATE 24
ACCESSION NUMBER: 1998340076 EMBASE Full-text
TITLE: Progress in the design of DNA sequence-specific

lexitropsins.
AUTHOR: Walker W.L.; Kopka M.L.; Goodsell D.S.
CORPORATE SOURCE: D.S. Goodsell, Department of Molecular Biology, Scripps Research Institute, San Diego, CA 92037, United States
SOURCE: Biopolymers - Nucleic Acid Sciences Section, (1997) 44/4 (323-334).
Refs: 44
ISSN: 0006-3525 CODEN: BNSSFF
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 022 Human Genetics
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:
Sequence-specific polyamides that bind in the minor ***groove*** of DNA are attractive candidates for antibiotics, cancer chemotherapeutics, and transcriptional antagonists. This paper reviews the progress of structure- based design of minor-groove-***binding*** polyamides, from the first structure of netropsin with DNA, to the effective linked polyamides currently under study. A theory of polyamide specificity is also reviewed, introducing methods to determine the optimal strategies for targeting a given ***DNA*** sequence within a genome of competing sequences.

L6 ANSWER 34 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:488700 CAPLUS Full-text
TITLE: Subnanomolar recognition of the minor groove of DNA by designed ligands.
AUTHOR(S): Turner, James M.; Baird, Eldon E.; Dervan, Peter B.
CORPORATE SOURCE: Division Chemistry and Chemical Engineering, California Institute Technology, Pasadena, CA, 91125, USA
SOURCE: Book of Abstracts, 214th ACS National Meeting, Las Vegas, NV, September 7-11 (1997), ORGN-300. American Chemical Society: Washington, D. C.
CODEN: 64RNAO
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
ABSTRACT:
Small mols. that specifically bind at subnanomolar concentration to any predetd. DNA sequence would be useful tools in mol. biol. and potentially in human medicine. The DNA sequence specificity of ***minor*** -groove-binding polyamides containing pyrrole and imidazole amino acids can be rationally controlled by simple pairing rules. We will report a ten-ring hairpin polyamide motif for subnanomolar recognition of 7 base pair (bp) sites. A novel β-alanine substituted hairpin motif will be presented for recognition of longer sequences.

L6 ANSWER 35 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:488699 CAPLUS Full-text
TITLE: Recognition of G,C-rich sequences in the minor groove of DNA.
AUTHOR(S): Swalley, Susanne E.; Baird, Eldon E.; Dervan, Peter B.
CORPORATE SOURCE: Division Chemistry and Chemical Engineering, California Institute Technology, Pasadena, CA, 91125, USA
SOURCE: Book of Abstracts, 214th ACS National Meeting, Las Vegas, NV, September 7-11 (1997), ORGN-299. American Chemical Society: Washington, D. C.
CODEN: 64RNAO
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
ABSTRACT:
Polyamides containing N-methylpyrrole and N-methylimidazole amino acids are synthetic ligands that have an affinity and specificity for DNA comparable to naturally occurring DNA-binding proteins. Pyrroleimidazole polyamides have recently been shown to be cell permeable and to inhibit the transcription of specific genes, providing impetus to explore the scope and limitations of this approach for ***DNA*** recognition. We will describe two different hairpin ***polyamide*** motifs capable of specifically binding G,C-rich six ***base*** pair sequences with subnanomolar affinities.

L6 ANSWER 36 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 25
ACCESSION NUMBER: 1997:245039 CAPLUS Full-text
DOCUMENT NUMBER: 126:326922
TITLE: Crystal structures of A-DNA duplexes
AUTHOR(S): Wahl, Markus C.; Sundaralingam, Muttaiya
CORPORATE SOURCE: Lab. Biological Macromoleuclar Structure, Ohio State Univ., Columbus, OH, 43210-1002, USA
SOURCE: Biopolymers (1997), 44(1), 45-63
CODEN: BIPMAA; ISSN: 0006-3525
PUBLISHER: Wiley
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
ABSTRACT:
A review with 97 refs. All crystal structures of A-DNA duplexes exhibit a typical crystal packing, with the termini of one mol. abutting the shallow grooves of symmetry related neighbors, while all other forms (B, Z, and ***RNA***) tend to form infinitely stacked helixes. The A-DNA arrangement leads to the formation of shallow groove base multiples that have implications for the structure of DNA in compacted states. The characteristic packing leaves big solvent channels, which can be sometimes occupied by B-DNA duplexes. Comparisons of the structures of the same oligomer crystallizing in two different space groups and of different sequences crystallizing in the same space group show that the lattice forces dominate the A-***DNA*** conformation in the crystals, complicating the effort to elucidate the influence of the base sequence on the structures. Nevertheless, in both alternating and nonalternating fragments some sequence effects can still be uncovered. Furthermore, several studies have started to define the minimal sequence changes or chemical modifications that can interconvert the oligomers between different double-helical conformers (A-, B-, and Z-form). Overall, it is seen that the rigid nucleotide principle applies to the oligomeric fragments. Besides the structures of the naked DNAs, their interactions with water, polyamines, and metal ions have attracted considerable attention. There are conserved patterns in the hydration, involving both the grooves and the backbone, which are different from those of B-DNA or Z-DNA. Overall, A-DNA seems to be more economically hydrated than B-DNA, particularly around the sugar-phosphate backbone. Spermine was found to be able to bind exclusively to either of the grooves or to the phosphate groups of the backbone, or exhibit a mixed binding mode. The located metal cations prefer binding to guanine bases and phosphate groups. The only mispairs investigated in A-DNA are the wobble pairs, yielding structural insight into their effects on helix stabilities and hydration. G·T wobble pairs have been determined in various sequence contexts, where they differentially affect the conformations and stableness of the duplexes. The structure of a G·mSC base pair, which surprisingly also adopted the wobble conformation, suggests that a similar geometry may transiently exist for G·C pairs. These results from the crystalline state will be compared to the solution state and discussed in relation to their relevance in biol.

L6 ANSWER 37 OF 98 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1997:429016 BIOSIS Full-text
DOCUMENT NUMBER: PREV199799728219
TITLE: Subnanomolar recognition of the minor groove of DNA by designed ligands.
AUTHOR(S): Turner, James M.; Baird, Eldon E.; Dervan, Peter B.
CORPORATE SOURCE: Div. Chem. Chem. Eng., Calif. Inst. Technol., Pasadena, CA 91125, USA
SOURCE: Abstracts of Papers American Chemical Society, (1997) Vol. 214, No. 1-2, pp. ORGN 300.
Meeting Info.: 214th American Chemical Society National Meeting. Las Vegas, Nevada, USA. September 7-11, 1997.
CODEN: ACSRAL. ISSN: 0065-7727.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 8 Oct 1997
Last Updated on STN: 8 Oct 1997

L6 ANSWER 38 OF 98 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1997:429015 BIOSIS Full-text
DOCUMENT NUMBER: PREV199799728218
TITLE: Recognition of G,C-rich sequences in the minor groove of DNA.
AUTHOR(S): Swalley, Susanne E.; Baird, Eldon E.; Dervan, Peter B.
CORPORATE SOURCE: Div. Chem. Chemical Eng., Calif. Inst. Technol., Pasadena, CA 91125, USA
SOURCE: Abstracts of Papers American Chemical Society, (1997) Vol. 214, No. 1-2, pp. ORGN 299.
Meeting Info.: 214th American Chemical Society National Meeting. Las Vegas, Nevada, USA. September 7-11, 1997.
CODEN: ACSRAL. ISSN: 0065-7727.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 8 Oct 1997
Last Updated on STN: 21 Nov 1997

L6 ANSWER 39 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 26
ACCESSION NUMBER: 1996:498677 CAPLUS Full-text

DOCUMENT NUMBER: 125:188569
TITLE: Binding of a hairpin polyamide in the minor groove of DNA: sequence-specific enthalpic discrimination
AUTHOR(S): Pilch, Daniel S.; Poklar, Natasa; Gelfand, Craig A.; Law, Scott M.; Breslauer, Kenneth J.; Baird, Eldon E.; Dervan, Peter B.
CORPORATE SOURCE: Dep. Chemistry, Rutgers-State Univ. New Jersey, New Brunswick, NJ, 08903, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1996), 93(16), 8306-8311
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Hairpin polyamides are synthetic ligands for sequence-specific recognition in the minor groove of double-helical ***DNA.*** A thermodn. characterization of the DNA-binding properties exhibited by a six-ring hairpin polyamide, ImPyPy-γ-PyPyPy-β-Dp (where Im = imidazole, Py = pyrrole, γ = γ-aminobutyric acid, β = β-alanine, and Dp = dimethylaminopropylamide), reveals an ≈1-2 kcal/mol greater affinity for the designated match site, 5'-TGTTA-3', relative to the single base ***pair*** mismatch sites, 5'-TGGTA-3' and 5'-TATTA-3'. The enthalpy and entropy data at 20° reveal this sequence specificity to be entirely enthalpic in origin. Correlations between the thermodn. driving forces underlying the sequence specificity exhibited by Im-PyPy-γ-PyPyPy-β-Dp and the structure properties of the heterodimeric complex of PyPyPy and ImPyPy bound to the minor groove of DNA provide insight into the mol. forces that govern the affinity and specificity of pyrrole-imidazole polyamides.

L6 ANSWER 40 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 27
ACCESSION NUMBER: 1996:494547 CAPLUS Full-text
DOCUMENT NUMBER: 125:188558
TITLE: Recognition of a 5'-(A,T)GGG(A,T)2-3' Sequence in the Minor Groove of DNA by an Eight-Ring Hairpin Polyamide
AUTHOR(S): Swalley, Susanne E.; Baird, Eldon E.; Dervan, Peter B.
CORPORATE SOURCE: Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, CA, 91125, USA
SOURCE: Journal of the American Chemical Society (1996), 118(35), 8198-8206
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
The use of pyrrole-imidazole polyamides for the recognition of core 5'-GGG-3' sequences in the minor groove of double stranded ***DNA*** is described. Two hairpin pyrrole-imidazole polyamides, ImImIm-γ-PyPyPy-β-Dp and ImImImPy-γ-PyPyPyPy-β-Dp (Im = N-methylimidazole-2-carboxamide, Py = N-methylpyrrole-2-carboxamide, β = β-alanine, γ = γ-aminobutyric acid, and Dp = ((dimethylamino)propyl)amide), as well as the corresponding EDTA affinity cleaving derivs., were synthesized and their DNA binding properties analyzed. Quant. DNase I footprint titrns. demonstrate that ImImIm-γ-PyPyPy-β-Dp binds the formal match sequence 5'-AGGGA-3' with an equilibrium association constant of Ka = 5+106 M-1 (10 mM Tris·HCl, 10 mM KCl, 10 mM MgCl2, and 5 mM CaCl2, pH 7.0 and 22°). ImImImPy-γ-PyPyPyPy-β-Dp binds the same site, 5'-AGGGAA-3', approx. two orders of magnitude more tightly than the six ring polyamide, with an equilibrium association constant of Ka = 4+108 M-1. The eight-ring hairpin polyamide demonstrates greater specificity for single base pair mismatches than does the six ring hairpin. Polyamides with an EDTA·Fe(II) moiety at the carboxy terminus confirm that the each hairpin binds in a single orientation. The high affinity recognition of a 5'-GGG-3' core sequence by an eight ring polyamide containing three contiguous imidazole amino acids demonstrates the versatility of pyrrole-imidazole polyamides and broadens the sequence repertoire for DNA recognition.

L6 ANSWER 41 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 28
ACCESSION NUMBER: 1996:421219 CAPLUS Full-text
DOCUMENT NUMBER: 125:160311
TITLE: Binding site size limit of the 2:1 pyrrole-imidazole polyamide-DNA motif
AUTHOR(S): Kelly, James J.; Baird, Eldon E.; Dervan, Peter B.
CORPORATE SOURCE: Chem. Eng., California Inst. Technol., Pasadena, CA, 91125, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1996), 93(14), 6981-6985
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Polyamides containing N-methylimidazole (Im) and N-methylpyrrole (Py) amino acids can be combined in antiparallel side-by-side dimeric complexes for sequence-specific recognition in the minor groove of ***DNA.*** Six polyamides containing three to eight rings bind ***DNA*** sites 5-10 bp in length, resp. Quant. DNase I footprint titration expts. demonstrate that affinity maximizes and is similar at ring sizes of five, six, and seven. Sequence specificity decreases as the length of the ***polyamides*** increases beyond five rings. These results provide useful guidelines for the design of new polyamides that bind longer DNA sites with enhanced affinity and specificity.

L6 ANSWER 42 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:379792 CAPLUS Full-text
DOCUMENT NUMBER: 125:51671
TITLE: Cooperative Triple-Helix Formation via a Sequence Specific Minor Groove Dimerization Domain
AUTHOR(S): Szewczyk, Jason W.; Baird, Eldon E.; Dervan, Peter B.
CORPORATE SOURCE: Arnold and Mabel Beckman Laboratories of Chemical Synthesis, California Institute of Technology, Pasadena, CA, 91125, USA
SOURCE: Journal of the American Chemical Society (1996), 118(28), 6778-6779
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
The energetics of cooperative binding of oligodeoxyribonucleotides via a sequence specific dimerization domain have been determined A pyrimidine oligonucleotide 11 bases in length covalently tethered to a three ring pyrrole-imidazole polyamide is found to bind cooperatively as a homodimer to a 31 base pair duplex DNA target site by simultaneous formation of a 2:1 polyamide-DNA complex in the minor groove and oligonucleotide directed triple helix formation in the major groove. The designed ***polyamide*** -oligonucleotide binds with 100-fold increased affinity relative to unlinked polyamide or oligonucleotide alone. No cooperativity is observed for a polyamide-oligonucleotide with a mismatch in the dimerization domain.

L6 ANSWER 43 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 29
ACCESSION NUMBER: 1996:354122 CAPLUS Full-text
DOCUMENT NUMBER: 125:51678
TITLE: Extension of Sequence-Specific Recognition in the Minor Groove of DNA by Pyrrole-Imidazole Polyamides to 9-13 Base Pairs
AUTHOR(S): Trauger, John W.; Baird, Eldon E.; Mrksich, Milan; Dervan, Peter B.
CORPORATE SOURCE: Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, CA, 91125, USA
SOURCE: Journal of the American Chemical Society (1996), 118(26), 6160-6166
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
The sequence-specific recognition of the minor groove of ***DNA*** by pyrrole-imidazole polyamides has been extended to 9-13 ***base*** pairs (bp). Four polyamides, ImPyPy-Py-PyPyPy-Dp, ImPyPy-G-PyPyPy-Dp, ImPyPy-β-PyPyPy-Dp, and ImPyPy-γ-PyPyPy-Dp (Im = N-methylimidazole, Py = N-methylpyrrole, Dp = dimethylaminopropylamide, G = glycine, β = β-alanine, and γ = γ-aminobutyric acid), were synthesized and characterized with respect to their DNA-binding affinities and specificities at sequences of composition 5'-(A,T)G(A,T)5C(A,T)-3' (9 bp) and 5'-(A,T)5G(A,T)C(A,T)5-3' (13 bp). In both sequence contexts, the β-alanine-linked compound ImPyPy-β-PyPyPy-Dp has the highest binding affinity of the four ***polyamides*** , binding the 9 bp site 5'-TGTTAAACA-3' (Ka = 8 + 108 M-1) and the 13 bp site 5'-AAAAAGACAAAAA-3' (Ka = 5 + 109 M-1) with affinities higher than the formally N-methylpyrrole-linked ***polyamide*** ImPyPy-Py-PyPyPy-Dp by factors of .apprx.8 and .apprx.85, resp. (10 mM Tris·HCl, 10 mM KCl, 10 mM MgCl2, and 5 mM CaCl2, pH 7.0).

The binding data for ImPyPy-γ-PyPyPy-Dp, which has been shown previously to bind DNA in a hairpin conformation, indicates that γ-aminobutyric acid does not effectively link polyamide subunits in an extended conformation. These results expand the binding site size targetable with pyrrole-imidazole polyamides and provide structural elements that will facilitate the design of new polyamides targeted to other DNA sequences.

L6 ANSWER 44 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 30
ACCESSION NUMBER: 1996:354123 CAPLUS Full-text
DOCUMENT NUMBER: 125:79645
TITLE: Recognition of 5'-(A,T)GG(A,T)2-3' Sequences in the Minor Groove of DNA by Hairpin Polyamides
AUTHOR(S): Parks, Michelle E.; Baird, Eldon E.; Dervan, Peter B.
CORPORATE SOURCE: Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, CA, 91125, USA
SOURCE: Journal of the American Chemical Society (1996), 118(26), 6153-6159
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
A series of four hairpin pyrrole-imidazole polyamides, ImImPy-γ-PyPyPy-β-Dp, PyPyPy-γ-ImImPy-β-Dp, AcImImPy-γ-PyPyPy-β-Dp, and AcPyPyPy-γ-ImImPy-β-Dp (Im = N-methylimidazole-2-carboxamide, Py = N-methylpyrrole-2-carboxamide, Dp = dimethylaminopropylamide, γ = γ-aminobutyric acid, β = β-alanine, and Ac = acetyl), designed for recognition of 5'-(A,T)GG(A,T)2-3' sequences in the minor groove of ***DNA*** were synthesized using solid phase methodol. and analyzed with respect to DNA binding affinity and sequence specificity. Quant. DNase I footprint titration expts. reveal that the optimal ***polyamide*** ImImPy-γ-PyPyPy-β-Dp binds a designated 5'-TGGTT-3' match site with an equilibrium association constant of Ka = 1.0 + 108 M-1 and the single base pair mismatch sites, 5'-TGTTA-3' and 5'-GGGTA-3', with 50-fold and 100-fold-lower affinity, resp. (10 mM Tris·HCl, 10 mM KCl, 10 mM MgCl2, and 5 mM CaCl2, pH 7.0 and 22 °C). Polyamides of sequence composition AcImImPy-γ-PyPyPy-β-Dp and AcPyPyPy-γ-ImImPy-β-Dp, which differ only by the position of the γ-linker, bind with similar affinities and specificities. Recognition of sequences containing contiguous G·C ***base*** pairs expands the sequence repertoire available for targeting DNA with pyrrole-imidazole polyamides.

L6 ANSWER 45 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 31
ACCESSION NUMBER: 1996:354121 CAPLUS Full-text
DOCUMENT NUMBER: 125:51677
TITLE: Optimization of the Hairpin Polyamide Design for Recognition of the Minor Groove of DNA
AUTHOR(S): Parks, Michelle E.; Baird, Eldon E.; Dervan, Peter B.
CORPORATE SOURCE: Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, CA, 91125, USA
SOURCE: Journal of the American Chemical Society (1996), 118(26), 6147-6152
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
In order to optimize the hairpin design for ligands which bind the ***minor*** groove of DNA, a series of four pyrrole-imidazole polyamides substituted at the C-terminus with aliphatic amino acids have been prepared using solid phase synthetic methodol. Addition of a C-terminal β-alanine residue is found to enhance both the ***DNA*** binding affinity and sequence specificity, while addition of a C-terminal glycine residue is found to reduce DNA binding affinity and sequence specificity. These effects are modulated by the addition of an N-terminal acetyl group. Insertion of a C-terminal aliphatic amino acid residue makes the hairpin polyamide motif compatible with solid phase synthetic methods, allowing the rapid design of new polyamides for high-affinity specific recognition of a broad sequence repertoire in the ***minor*** groove of DNA.

L6 ANSWER 46 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 32
ACCESSION NUMBER: 1996:354120 CAPLUS Full-text
DOCUMENT NUMBER: 125:168615
TITLE: Solid Phase Synthesis of Polyamides Containing Imidazole and Pyrrole Amino Acids
AUTHOR(S): Baird, Eldon E.; Dervan, Peter B.
CORPORATE SOURCE: Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, CA, 91125, USA
SOURCE: Journal of the American Chemical Society (1996), 118(26), 6141-6146
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
The solid phase synthesis of sequence specific DNA binding ***polyamides*** containing N-methylimidazole (Im) and N-methylpyrrole (Py) amino acids is described. Two monomer building blocks, Boc-Py-OBt ester and Boc-Im acid, are prepared on a 50 g scale without column chromatog. Using com. available Boc-β-alanine-Pam resin, cycling protocols were optimized to afford high stepwise coupling yields (>99%). Deprotection by aminolysis affords up to 100 mg quantities of polyamide. Solid phase methodol. increases both the number and complexity of minor groove ***binding*** polyamides which can be synthesized and analyzed with regard to DNA binding affinity and sequence specificity. The solid phase synthesis of a representative eight-residue polyamide is reported.

L6 ANSWER 47 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 33
ACCESSION NUMBER: 1996:344880 CAPLUS Full-text
DOCUMENT NUMBER: 125:28430
TITLE: Interactions of spermidine and methylspermidine with DNA studied by nuclear magnetic resonance self-diffusion measurements
AUTHOR(S): Andreasson, Bo; Nordenskioeld, Lars; Schultz, Johan
CORPORATE SOURCE: Division of Physical Chemistry, University of Stockholm, Stockholm, S-10691, Swed.
SOURCE: Biophysical Journal (1996), 70(6), 2847-2856
CODEN: BIOJAU; ISSN: 0006-3495
PUBLISHER: Biophysical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
The NMR pulsed field gradient self-diffusion method has been used to study the self-diffusion of the polyamine spermidine and the polyamine analog methylspermidine (completely N-methylated spermidine). The self-diffusion coefficient, D, was measured in solns. of calf thymus DNA prepared from nucleosome core particles (with an average length of 120 base ***pairs***) as a function of the concentration ratio of polyamine to ***DNA*** phosphate. A study of the self-diffusion quotient, D/Do (where Do is the diffusion coefficient for free polyamine, not associated with ***DNA***), in addns. of spermidine and methylspermidine to solns. of NaDNA/NaCl, gave almost identical results with complete association of ***polyamine*** to DNA in the initial part of the titrns., indicating similar affinities for DNA. A large influence on the measured self-diffusion coeffs. was detected for methylspermidine in NaDNA solns. with different concns. of NaCl, which shows a considerable salt effect on the polyamine-DNA association No notable differences in D/Do for methylspermidine were observed in competitive titrns. of solns. of Li- and NaDNA, indicating that sodium and lithium ions behave similarly in their interactions with DNA. In titration expts. of methylspermidine into MgDNA solution, the results showed that the polyamine association is less effective than in the case of NaDNA, because of competition from magnesium ***binding*** to DNA. Comparisons with calcns. based on the electrostatic Poisson-Boltzmann cell model were performed. It is suggested that the interaction is primarily of electrostatic nature, with no ***binding*** to specific sites on the DNA mol.

L6 ANSWER 48 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:473406 CAPLUS Full-text
DOCUMENT NUMBER: 125:135683
TITLE: Sequence-specific recognition of DNA by a major and minor groove binding ligand
AUTHOR(S): Szewczyk, Jason W.; Baird, Eldon E.; Dervan, Peter B.
CORPORATE SOURCE: Arnold and Mabel Beckman Lab. Chem. Synthesis, California Inst. Technology, Pasadena, CA, 91125, USA
SOURCE: Angewandte Chemie, International Edition in English (1996), 35(13/14), 1487-1489
CODEN: ACIEAY; ISSN: 0570-0833
PUBLISHER: VCH
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
The authors report here that hairpin polyamide linked to an 11-mer oligonucleotide specifically and simultaneously binds the ***major*** and minor grooves of DNA at sub

nanomolar concentration

L6 ANSWER 49 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 34
ACCESSION NUMBER: 1996:463869 CAPLUS Full-text
DOCUMENT NUMBER: 125:161351
TITLE: Simultaneous binding of a polyamide dimer and an oligonucleotide in the minor and major grooves of DNA
AUTHOR(S): Parks, Michelle E.; Dervan, Peter B.
CORPORATE SOURCE: Div. Chem. Chem. Eng., California Inst. of Technology, Pasadena, CA, 91125, USA
SOURCE: Bioorganic & Medicinal Chemistry (1996), 4(7), 1045-1050
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
The effect of the polyamide ImPyPy-Dp (Im = N-methylimidazole-2-carboxamide, Py = N-methylpyrrole-2-carboxamide, and Dp = dimethylaminopropylamide), which binds as an antiparallel dimer in the Watson-Crick minor groove, on pyrimidine·purine·pyrimidine triple helix stability was investigated. A DNA restriction fragment was designed which contained two triple helix sites, one of which overlapped a minor ***groove*** ligand site (proximal), and a control site 13 base ***pairs*** away (distal). Using quant. DNase I footprint titration expts. the equilibrium association constant of oligonucleotide 5'-TTTTTm5CTTTm5CTTTm5CT-3' to each site was measured in the absence and presence of the polyamide dimer. The data indicate that triple helix formation is compatible with a ***polyamide*** dimer binding in the minor groove of DNA at an overlapping site. No cooperative effect of the ***polyamide*** dimer on the equilibrium association constant of the oligonucleotide was observed

L6 ANSWER 50 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 35
ACCESSION NUMBER: 1996:432294 CAPLUS Full-text
DOCUMENT NUMBER: 125:108019
TITLE: A microgonotropen pentaaza pentabutylamine and its interactions with DNA
AUTHOR(S): Sengupta, Dipanjan; Blasko, Andrei; Bruice, Thomas C.
CORPORATE SOURCE: Dep. Chem., Univ. California, Santa Barbara, CA, 93106, USA
SOURCE: Bioorganic & Medicinal Chemistry (1996), 4(6), 803-813
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 125:108019
ABSTRACT:
The central pyrrole of a site-selective DNA minor ***groove*** binding tripyrrole peptide (1) has been attached to N-protected pentaazapentacosanoic acid (17) via a -(CH2)3-NHCO-(CH2)3-linker to provide 19, subsequent deprotection provided the pentaaza microgonotropen 4. The polyamine moiety of 4 reaches out of the minor ***groove*** and binds to the phosphate backbone of DNA. We find when employing Hoechst 33258 (Ht) as fluorescent titrant to follow ***binding*** of 4 to the hexadecameric duplex d(GGCGCAAATTTGGCGG)/(CCGCCAAAT TTGCGCC) and by 1H NMR titration of d(CGCAAATTTGCG)2 with 4 that the latter forms both 1:1 and 2:1 dsDNA complexes. Certain aspects of the structure of 4:d(CGCAAATTTGCG)2 complex derived via 1H NMR are discussed. The electrophoretic mobilities of ϕX-174 DNA digested with HaeIII endonuclease restriction fragments complexed to 4 shows that the latter brings about a greater conformational change in the DNA fragments than observed previously with other microgonotropens.

L6 ANSWER 51 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 36
ACCESSION NUMBER: 1996:495062 CAPLUS Full-text
DOCUMENT NUMBER: 125:161376
TITLE: Recognition of DNA by designed ligands at subnanomolar concentrations
AUTHOR(S): Trauger, John W.; Baird, Eldon E.; Dervan, Peter B.
CORPORATE SOURCE: Div. Chem. Chem. Eng., California Inst. Technol., Pasadena, CA, 91125, USA
SOURCE: Nature (London) (1996), 382(6591), 559-561
CODEN: NATUAS; ISSN: 0028-0836
PUBLISHER: Macmillan Magazines
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Small mols. that specifically bind with high affinity to any predetd. ***DNA*** sequence in the human genome would be useful tools in mol. biol. and potentially in human medicine. Simple rules have been developed to control rationally the sequence specificity of minor-groove-***binding*** polyamides containing N-methylimidazole and N-methylpyrrole amino acids. Two eight-ring pyrrole-imidazole ***polyamides*** differing in sequence by a single amino acid bind specifically to resp. six-base-pair target sites which differ in sequence by a single base pair. Binding is observed at subnanomolar concns. of ligand. The replacement of a single nitrogen atom with a C-H regulates affinity and specificity by two orders of magnitude. The broad range of sequences that can be specifically targeted with pyrrole-imidazole polyamides, coupled with an efficient solid-phase synthesis methodol., identify a powerful class of small mols. for sequence-specific recognition of double-helical DNA.

L6 ANSWER 52 OF 98 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 96:234820 SCISEARCH Full-text
THE GENUINE ARTICLE: UA092
TITLE: AN NMR SELF-DIFFUSION STUDY OF THE INTERACTIONS BETWEEN SPERMIDINE AND OLIGONUCLEOTIDES
AUTHOR: ANDREASSON B; NORDENSKIOLD L (Reprint); BRAUNLIN W H
CORPORATE SOURCE: UNIV STOCKHOLM, DIV PHYS CHEM, S-10691 STOCKHOLM, SWEDEN (Reprint); UNIV STOCKHOLM, DIV PHYS CHEM, S-10691 STOCKHOLM, SWEDEN; UNIV NEBRASKA, DEPT CHEM, LINCOLN, NE, 68588
COUNTRY OF AUTHOR: SWEDEN; USA
SOURCE: BIOPOLYMERS, (APR 1996) Vol. 38, No. 4, pp. 505-513. ISSN: 0006-3525.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 35
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
ABSTRACT:
Self-diffusion coefficients have been determined by pulsed field gradient nmr methods for spermidine in solutions of the oligonucleotides d(GC)(4) and d(GGAATTCC). The self-diffusion behavior of spermidine in solution of d(GC)(4) is very similar to that observed previously for methylspermidine (completely N-methylated spermidine). Moreover, the self-diffusion behaviors of spermidine in solutions of d(GC)(4) and d(GGAATTCC) are also quite similar, indicating that there is no significant influenceon on self-diffusion of oligonucleotide base composition. Furthermore, self-diffusion coefficients of the oligonucleotide d(GC)(8) show only a small dependence on oligonucleotide concentration, and no measurable dependence on sodium ion or magnesium ion concentration. (C) 1996 John Wiley & Sons, Inc.

L6 ANSWER 53 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 37
ACCESSION NUMBER: 1996:386564 CAPLUS Full-text
DOCUMENT NUMBER: 125:108335
TITLE: Extended hairpin polyamide motif for sequence-specific recognition in the minor groove of DNA
AUTHOR(S): Trauger, John W.; Baird, Eldon E.; Dervan, Peter B.
CORPORATE SOURCE: Arnold and Mabel Beckman Lab. Chem. Synthesis, California Inst. Technol., Pasadena, CA, 91125, USA
SOURCE: Chemistry & Biology (1996), 3(5), 369-377
CODEN: CBOLE2; ISSN: 1074-5521
PUBLISHER: Current Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Three-ring polyamides containing N-methylimidazole and N-methylpyrrole amino acids bind sequence-specifically to double-helical DNA by forming side-by-side complexes in the minor groove. Simple pairing rules relate the amino-acid sequence of a pyrrole-imidazole ***polyamide*** to its expected DNA target site, and ***polyamides*** that target a wide variety of DNA sequences have been synthesized. We have shown previously that two three-ring subunits could be linked together by an aliphatic amino acid, increasing the binding affinity of the polyamide and, in some cases, increasing the length of the target sequence. We set out to determine whether different types of linkers could be used in a single mol. to generate a nine-ring polyamide mol. that would bind to specific DNA sequences. A nine-ring pyrrole-imidazole polyamide, containing two different amino acid linkers, β-alanine and γ-aminobutyric acid, has been synthesized and shown to specifically bind a designated nine-base-pair target site at subnanomolar concentration in a novel extended hairpin conformation. The amino acids γ-aminobutyric acid and β-alanine optimally link three-ring pyrrole-imidazole subunits in 'hairpin' and 'extended' conformations, resp. Both aliphatic amino acids can be combined to generate a nine-ring polyamide that specifically recognizes a nine-base-pair target site with very high affinity.

L6 ANSWER 54 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 38
ACCESSION NUMBER: 1997:13785 CAPLUS Full-text

DOCUMENT NUMBER: 126:139546
TITLE: Selective DNA binding of(N-alkylamine)-substituted naphthalene imides and diimides to G+C-rich DNA
AUTHOR(S): Liu, Zhi-Ren; Hecker, Karl H.; Rill, Randolph L.
CORPORATE SOURCE: Dep.Chem. Inst. Mol. Biophysics, Florida State Univ., Tallahassee, FL, 32306-3006, USA
SOURCE: Journal of Biomolecular Structure & Dynamics (1996), 14(3), 331-339
CODEN: JBSDD6; ISSN: 0739-1102
PUBLISHER: Adenine Press
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:

Alkylamine-substituted naphthalene imides and diimides bind ***DNA*** by intercalation and have applications as anticancer agents. The unique structures of these imides in which two adjacent carbonyl groups lie coplanar to an extended aromatic ring system allow the possibility of sequence-selective interactions between the intercalated chromophore and guanine amino groups situated in the DNA minor ***groove.*** The binding affinities of N-[3-(dimethylamino)propylamine]-1,8-naphthalenedicarboxylic imide (N-DMPrNI) and N,N'-bis[3,3'-(dimethylamino)propylamine]-naphthalene-1,4,5,8-tetracarboxylic diimide (N-BDMPrNDI) for natural DNAs of differing base composition were determined spectroscopically and by equilibrium dialysis. In agreement with the above proposition, binding studies indicated that both the naphthalene imide and diimide strongly prefer to intercalate into steps containing at least one G:C base pair. The dependencies of association consts. on DNA base composition are consistent with a requirement for one G:C pair in the binding site of the monoimide, and two G:C pairs in ***binding*** sites of the diimide. These selectivities are comparable to or exceed that of actinomycin D, a classic G:C-selective drug. Protection footprinting with DNase I confirmed that the naphthalene monoimide (N-DMPrNI) prefers to bind adjacent to G:C base pairs, with a most consistent preference for "mixed" steps containing both a G:C and an A:T pair, excepting GA:TC. Several 5'-CG-3' steps were also good binding sites as indicated by nuclease protection, but few GC:GC or GG:CC steps were protected. The naphthalene diimide inhibited DNase I digestion, but did not yield a footprint. The base recognition ability and versatile chemical make naphthalene imides and diimides attractive building blocks for design of highly sequence-specific, DNA-directed drug candidates including conjugated oligonucleotides or oligopeptides.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 55 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:212462 CAPLUS Full-text
DOCUMENT NUMBER: 124:253634
TITLE: Extending the recognition site of designed minor groove binding molecules
AUTHOR(S): Geierstanger, Bernhard H.; Mrksich, Milan; Dervan, Peter B.; Wemmer, David E.
CORPORATE SOURCE: Dep. Chemistry, Univ. California, Berkeley, CA, 94720-1460, USA
SOURCE: Nature Structural Biology (1996), 3(4), 321-4
CODEN: NSBIEW; ISSN: 1072-8368
PUBLISHER: Nature Publishing Co.
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:

A linked, imazole/pyrrole minor-groove ligand has been shown to bind sequence specifically to a 13 base-pair target sequence in a mixed 1:1/2:1 mode.

L6 ANSWER 56 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 39
ACCESSION NUMBER: 1996:726918 CAPLUS Full-text
DOCUMENT NUMBER: 126:28158
TITLE: Interaction between left-handed Z-DNA and polyamine - 3. The crystal structure of the d(CG)3 and thermospermine complex
AUTHOR(S): Ohishi, Hirofumi; Terasoma, Noriko; Nakanishi, Isao; van der Marel, Gijs; van Boom, Jacques H.; Rich, Alexander; Wang, Andrew H.-J.; Hakoshima, Toshio; Tomita, Ken-ichi
CORPORATE SOURCE: Osaka University of Pharmaceutical Sciences, 4-20-1 Nasahara, Takatsuki, Osaka, 569-11, Japan
SOURCE: FEBS Letters (1996), 398(2,3), 291-296
CODEN: FEBLAL; ISSN: 0014-5793
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:

The DNA fragment, d(CG)3, was co-crystallized with N-(3-amino-propyl)-N-(5-aminopropyl)-1,4-diaminobutane (thermospermine; PA(334)), a polyamine metabolized from the nucleic acid. By using a good crystal with dimensions of 0.5+0.5+0.5 mm3, x-ray intensity data were collected up to 1.0 Å resolution. Two thermospermine mols. and a magnesium cation were bound to the left-handed double-helical d(CG)3 mol. The d(CG)3 mol. adopted the left-handed Z-conformation and two thermospermine mols. and a magnesium cation neutralized the neg. charges of the phosphate groups of the d(CG)3 mol. Furthermore, the binding modes between d(CG)3 and thermospermine were different from those of d(CG)3 complexes with PA(24), spermidine and spermine. This is the first case in which it was determined by x-ray crystallog. anal. that one of two thermospermine mols. bound three d(CG)3 duplexes which were sym. related to each other, and the other formed two hydrogen bonds at the N(5) and N(9) atoms with two adjacent nucleotide phosphate groups of a single d(CG)3 strand at the minor groove. Furthermore, no direct coordination bond was found between the d(CG)3 mol. and the magnesium cation.

L6 ANSWER 57 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 40
ACCESSION NUMBER: 1996:411436 CAPLUS Full-text
DOCUMENT NUMBER: 125:104281
TITLE: Cytotoxicity and antineoplastic activities of alkylamines and their borane derivatives
AUTHOR(S): Hall, Iris H.; Tse, Elaine Y.; Muhammad, Rosallah A.
CORPORATE SOURCE: Div. Medicinal Chem. Natural Products, School Pharmacy, Univ. North Carolina, Chapel Hill, NC, 27599-7360, USA
SOURCE: Metal-Based Drugs (1996), 3(2), 101-112
CODEN: MBADEI; ISSN: 0793-0291
PUBLISHER: Freund
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:

The alkylamines and their related boron derivs. demonstrated potent cytotoxicity against the growth of murine and human tissue cultured cells. These agents did not necessarily require the boron atom to possess potent cytotoxic action in certain tumor lines. Their ability to suppress tumor cell growth was based on their inhibition of DNA and protein syntheses. DNA synthesis was reduced because purine synthesis was blocked at the enzyme site of IMP dehydrogenase by the agents. In addition ribonucleotide reductase and nucleoside kinase activities were reduced by the agents which would account for the reduced d[NTP] pools. The DNA template or mol. may be a target of the drugs with regard to binding of the drug to nucleoside bases or intercalation of the drug between ***DNA*** base pairs. Only some of the agents caused ***DNA*** fragmentation with reduced DNA viscosity. These effects would contribute to overall cell death afforded by the agents.

L6 ANSWER 58 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 41
ACCESSION NUMBER: 1995:892660 CAPLUS Full-text
DOCUMENT NUMBER: 124:48499
TITLE: Cyclic polyamides for recognition in the minor groove of DNA
AUTHOR(S): Cho, Junhyeong; Parks, Michelle E.; Dervan, Peter B.
CORPORATE SOURCE: Beckman Inst., California Inst. Technol., Pasadena, CA, 91125, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1995), 92(22), 10389-92
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:

Small mols. that specifically bind with high affinity to any designated DNA sequence in the human genome would be useful tools in mol. biol. and potentially in human medicine. Simple rules have been developed to rationally alter the sequence specificity of minor groove -binding polyamides containing N-methylimidazole and N-methylpyrrole amino acids. Crescent-shaped polyamides bind as antiparallel dimers with each polyamide making specific contacts with each strand on the floor of the minor groove. Cyclic ***polyamides*** have now been synthesized that bind designated ***DNA*** sequences at subnanomolar concns.

L6 ANSWER 59 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 42
ACCESSION NUMBER: 1995:826879 CAPLUS Full-text
DOCUMENT NUMBER: 124:24074
TITLE: Selective Stabilization of DNA Triple Helixes by Benzopyridoindole Derivatives
AUTHOR(S): Escude, Christophe; Nguyen, Chi Hung; Mergny, Jean-Louis; Sun, Jian-Sheng; Bisagni, Emile; Garestier, Therese; Helene, Claude
CORPORATE SOURCE: Laboratoire de Biophysique, Museum National d'Histoire Naturelle, Paris, 75231, Fr.
SOURCE: Journal of the American Chemical Society (1995), 117(41), 10212-19

CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
A major challenge in the use of oligonucleotides in an anti-gene strategy is to stabilize triple helix formation under physiol. conditions. A benzo[e]pyridoindole derivative was shown earlier to stabilize triple-helical better than double-helical complexes (Mergny, J. L. et al. Science 1992, 256, 1681-1684). New derivs. of the benzopyridoindole family were synthesized, and their ability to stabilize triple helixes was investigated by thermal denaturation expts. using UV absorption spectroscopy. The stabilizing effects of all the available derivs. were compared and allowed us to infer some general rules regarding the role of the geometry of the mol. and of its various substituents. The melting temperature (Tm) of the triplex-to-duplex transition is increased from 18 to 49°C (ΔTmax = +31°C) upon ***binding*** of 3-methoxy-10-methyl-7-[3-(N-methyl-N-3-aminopropyl)propyl]amino-11H-benzo[g]pyrido[4,3-b]indole (BgPI), in a 10 mM sodium cacodylate buffer (pH 6.2) containing 0.1 M NaCl. Sequence-specific effects were also investigated. Benzo[e]- and benzo[g]pyrido[4,3-b]indole derivs. exhibited different properties regarding the role of the alkylamine side chain attached to the pyridine ring. Effects of these compds. on the melting of duplex DNA were also sensitive to changes in the chemical nature of the alkylamine side chain. Results are discussed in terms of resp. affinities for triplex and duplex structures. A model is proposed to explain the different roles played by the alkylamine side chain for both types of mols. For the benzo[e]pyridoindole derivs., the chain is suggested to lie in the major groove of the triple helix, whereas for the benzo[g]pyridoindole derivs., it lies in the minor ***groove.*** These results provide an exptl. and theor. basis for understanding intercalation of dyes in triple helixes and should help to conceive more specific triple helix ligands and to design oligonucleotide-***intercalator*** conjugates for stable triple helix formation.

L6 ANSWER 60 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 43
ACCESSION NUMBER: 1995:663749 CAPLUS Full-text
DOCUMENT NUMBER: 123:104203
TITLE: Base-pair opening and spermine binding - B-DNA features displayed in the crystal structure of a gal operon fragment: implications for protein-DNA recognition
AUTHOR(S): Tari, Leslie W.; Secco, Anthony S.
CORPORATE SOURCE: Dep. Chem., Univ. Manitoba, Winnipeg, MB, R3T 2N2, Can.
SOURCE: Nucleic Acids Research (1995), 23(11), 2065-73
CODEN: NARHAD; ISSN: 0305-1048
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
A sequence that is represented frequently in functionally important sites involving protein-DNA interactions is GTG/CAC, suggesting that the trimer may play a role in regulatory processes. The 2.5 Å resolution structure of d(CGGTGG)/d(CCACCG), a part of the interior operator (OI, nucleotides +44 to +49) of the gal operon, co-crystallized with spermine, is described herein. The crystal packing arrangement in this structure is unprecedented in a crystal of B-DNA, revealing a close packing of columns of stacked DNA resembling a 5-stranded twisted wire cable. The final structure contains one hexamer duplex, 17 water mols. and 1.5 spermine mols. per crystallog. asym. unit. The hexamer exhibits base -pair opening and shearing at T·A resulting in a novel non-Watson-Crick hydrogen-bonding scheme between adenine and thymine in the GTG region. The ability of this sequence to adopt unusual conformations in its GTG region may be a critical factor conferring sequence selectivity on the ***binding*** of Gal repressor. In addition, this is the first conclusive example of a crystal structure of spermine with native B-DNA, providing insight into the mechanics of polyamine-DNA ***binding*** , as well as possible explanations for the biol. action of spermine.

L6 ANSWER 61 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 44
ACCESSION NUMBER: 1996:57674 CAPLUS Full-text
DOCUMENT NUMBER: 124:110409
TITLE: Peptide nucleic acid (PNA): a model structure for the primordial genetic material?
AUTHOR(S): Nielsen, Peter E.
CORPORATE SOURCE: Dep. Biochem. B, Panum Inst., Copenhagen, Den.
SOURCE: Microbiologia (Madrid) (1995), 11(2), 209-16
CODEN: MICBE3; ISSN: 0213-4101
PUBLISHER: Garsi
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
The authors have recently described a novel DNA analog, peptide nucleic acid (PNA), which is relevant for the discussion of the origin of life. PNA consists of a pseudo-peptide (polyamide) backbone comprised of (2-aminoethyl)glycine units to which nucleobases are attached via carbonyl methylene linkers. The authors have found that PNA binds to oligo(deoxy)-ribonucleotides obeying the Watson-Crick base pairing rules, i.e., A-T and G-C base pairs are highly preferred. Thus in a chemical sense (but not in a functional one) PNA bridges the gap between proteins and nucleic acids. The results obtained with PNA clearly show that mols. with the potential of carrying genetic information are not required to obtain either phosphates or sugars but could be "peptides". It should be emphasized that although the authors have shown that PNA with the (2-aminoethyl)glycine backbone is an amazingly good mimic of DNA, the authors do not yet know the structural constraints within which this property exists. Recent results have shown, however, that extending the backbone by using β-alanine in place of glycine is deleterious for PNA/DNA complex stability. It can be argued that the optimal backbone for a genetic material is not necessarily the backbone that gives the most stable duplex. Indeed, if the duplex is too stable, the genetic information is not available for transcription and replication processes. It is proposed that the primordial genetic material could have been PNAs, i.e., DNA analogs having a peptide backbone. PNA monomers based on the amino acids α,γ-diaminobutyric acid or ornithine are suggested as compds. that could have been formed in the prebiotic soup. Finally, the possibility of a PNA/RNA world is presented, in which PNA constitutes the stable genetic material, while ***RNA*** , which may be polymerized using the PNA as template, accounts for enzymic activities, including PNA replication.

L6 ANSWER 62 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 45
ACCESSION NUMBER: 1994:502210 CAPLUS Full-text
DOCUMENT NUMBER: 121:102210
TITLE: Bending and Straightening of DNA Induced by the Same Ligand: Characterization with the Atomic Force Microscope
AUTHOR(S): Hansma, Helen G.; Browne, Kenneth A.; Bezanilla, Magdalena; Bruice, Thomas C.
CORPORATE SOURCE: Department of Physics, University of California, Santa Barbara, CA, 93106, USA
SOURCE: Biochemistry (1994), 33(28), 8436-41
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
A new ligand, MGT-6b, binds to DNA with two linked parts: a ***polyamine*** that binds to the phosphate backbone and a tripyrrole peptide that binds to the minor groove . This ligand decreases the curvature of bent kinetoplast DNA (kDNA)and also increases the curvature of a 400-bp DNA that is used as a mol. weight standard (M400), as characterized with the atomic force microscope (AFM). MGT-6b is more effective than distamycin at straightening kDNA. MGT-6b retards the electrophoretic mobility of M400 DNA, although neither of its two component parts alters the mobility of M400 or its curvature as seen in the AFM. Thus, both parts of the ligand are needed for the "vise grip" mode of ***binding*** that affects DNA bending. The ability of MGT-6b to both bend and straighten DNA is probably related to the very different DNA sequences and, hence, structures of kDNA and M400 ***DNA.***

L6 ANSWER 63 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 46
ACCESSION NUMBER: 1994:317887 CAPLUS Full-text
DOCUMENT NUMBER: 120:317887
TITLE: Microgonotropens and Their Interactions with DNA. 5. Structural Characterization of the 1:1 Complex of d(CGCAAATTTGCG)2 and Tren-Microgonotropen-b by 2D NMR Spectroscopy and Restrained Molecular Modeling
AUTHOR(S): Blasko, Andrei; Browne, Kenneth A.; Bruice, Thomas C.
CORPORATE SOURCE: Department of Chemistry, University of California, Santa Barbara, CA, 93106, USA
SOURCE: Journal of the American Chemical Society (1994), 116(9), 3726-37
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Tren-microgonotropen-b (6b) binds 1:1 and 2:1 into the minor ***groove*** of d(CGCAAATTTGCG)2. The solution structure of the 1:1 complex of d(CGCA3T3GCG)2 with 6b has been determined by 2D nuclear Overhauser effect 1H NMR spectroscopy (NOESY) and restrained mol. modeling. An 1H NMR melting study on d(CGCA3T3GCG)2 shows that while the G·C base pairs exist equally as paired and melted forms at 35°C, the A3T3 region maintains base pairing up to 45°C. A total of 206 resonances for the d(CGCA3T3GCG)2:6b have been assigned. The signals of both exchangeable and nonexchangeable protons in the NOESY spectra indicate asym. binding

of 6b in the A + T-rich region involving five base pairs (5'-A6T7T8T9G10-3'). The amino terminal acetamide head of 6b is directed toward A6, while the carboxy terminal dimethylpropylamino tail is directed toward G10. The protonated tren polyamino substituent residing on the nitrogen of the central pyrrole ring is directed up toward the phosphate backbone, firmly grasping the phosphodiester linkages of P9 and P10 on the edge of the major groove. The protonated terminal nitrogen of the dimethylpropylamino tail is adjacent to sugar oxygen C1104' and a base oxygen C1102 within the minor groove. The off-rate of 6b from the 1:1 complex was found to be 1.3 ± 0.2 s-1, corresponding to an activation energy of 17 kcal/mol. Compound 6b binds 3.1-4.5 Å from the bottom of the minor groove and 7.3-9.0 and 5.5-6.4 Å distant from the (-) and (+) strands, resp. when observing the strands of the DNA in a 5' to 3' orientation (distances from the pyrrole nitrogens to P-4P-5P-6 and P8P9P10, resp.). Comparisons of the solution structures of d(CGCA3T3GCG)2 and the d(CGCA3T3GCG)2:6b complex with the crystal structure of the same dsDNA, show that there is a break in the C2v symmetry of the crystallized dsDNA at the A6T7 junction as it goes into aqueous solution A helical bend, α, of 22.2° was found for the solution structure of the d(CGCA3T3GCG)2:6b complex; this is an increase of 11.4° relative to the crystallized dodecamer (α = 10.8°), 8.3°relative to the crystallized d(CGCA3T3GCG)2:distamycin complex (α = 13.9°) and 5.0° relative to the solution structure of d(CGCA3T3GCG)2:5c complex (α = 17.2°). In addition, solvation increases the length of the duplex by 0.2 Å/bp for the d(CGCA3T3GCG)2:6b complex compared to crystal structures of d(CGCA3T3GCG)2 and of the d(CGCA3T3GCG)2:distamycin complex. The A·T region of the d(CGCA3T3GCG)2:6b complex maintains its B-DNA conformation, while the terminal G·C ends appear to exist in an intermediate B- to A-DNA form.

L6 ANSWER 64 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 47
ACCESSION NUMBER: 1994:625316 CAPLUS Full-text
DOCUMENT NUMBER: 121:225316
TITLE: Analyzing DNA complexes by circular and linear dichroism
AUTHOR(S): Norden, Bengt; Kurucsev, Tomas
CORPORATE SOURCE: Dep. Physical Chem., Chalmers Univ. Technology, Goeteborg, S-142 96, Swed.
SOURCE: Journal of Molecular Recognition (1994), 7(2), 141-55
CODEN: JMORE4; ISSN: 0952-3499
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
ABSTRACT:
A review with many refs. Application of linear dichroism (LD) and CD in nucleic acid research is illustrated by recent results aimed at answering specific structural problems in the interaction of DNA with mols. of biol. importance. The authors first consider the circumstances under which ligands, such as DAPI (4',6-diamidino-2-phenylindole), change their preferred ***binding*** mode in the minor groove to major ***groove*** binding or intercalation. As an extension of this problem the authors refer to the switch between groove binding and intercalation of structurally similar ligands such as ellipticines and trigonal ruthenium complexes. They also explore the use of LD and CD in determination of the structure of the complex formed between the polynucleotide poly(dA) and the novel 'peptide nucleic acid', consisting of nucleic acid bases joined by a polyamide homomorphous with the deoxyribose-phosphate backbone of DNA. Finally, the structure and interaction of the recombination enzyme RecA with DNA is discussed, *in particular* the influence of the presence of intercalators, groove ***binders*** or covalent DNA adducts.

L6 ANSWER 65 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 48
ACCESSION NUMBER: 1995:102355 CAPLUS Full-text
DOCUMENT NUMBER: 122:181054
TITLE: The interaction of intercalators and groove-binding agents with DNA triple-helical structures: the influence of ligand structure, DNA backbone modifications and sequence
AUTHOR(S): Wilson, W. D.; Mizan, Shaikh; Tanious, Farial A.; Yao, Shijie
CORPORATE SOURCE: Dep. Chem., Georgia State Univ., Atlanta, GA, 30303, USA
SOURCE: Journal of Molecular Recognition (1994), 7(2), 89-98
CODEN: JMORE4; ISSN: 0952-3499
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
ABSTRACT:
A review with 56 refs. The effects of ligand structure and properties, ***DNA*** backbone modifications and DNA sequence on the interaction of a variety of well-known groove-binding agents and ***intercalators*** with DNA duplexes and triplexes have been evaluated by thermal melting expts. and mol. modeling. Both methylphosphonate and phosphorothioate substitutions generally destabilize DNA duplexes and triplexes. Modified duplexes can be strongly stabilized by both groove-***binding*** agents and intercalators, whereas triplexes are primarily stabilized by intercalators. Mol. modeling studies suggest that the large intercalating ring system of coralyne stacks well with the triplex bases, whereas the alkylamino side chain of quinacrine fits snugly into the remaining space of the major groove of dT19·dA19·dT19 triplex and forms extensive van der Waals contacts with the thymine Me groups that line the groove. Converting some of the T·A·T base triplets to C+·G·C (e.g., dT19·dA19·dT19 to d(T4C+)3T4·d(A4G)3A4·(T4C3)T4) causes very significant decreases in observed Tm increases for compds. such as quinacrine and coralyne. Although removal of thymine Me groups and addition of pos. charge on substitution of C+·G·C for T·A·T should reduce binding of cationic intercalators, the large difference observed between the pure AT and the mixed sequence triplexes suggest that they may also have differences in structure and properties.

L6 ANSWER 66 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 49
ACCESSION NUMBER: 1993:600288 CAPLUS Full-text
DOCUMENT NUMBER: 119:200288
TITLE: Polyamine and polyamine analog regulation of spermidine/spermine N1-acetyltransferase in MALME-3M human melanoma cells
AUTHOR(S): Fogel-Petrovic, Mirjana; Shappell, Nancy W.; Bergeron, Raymond J.; Porter, Carl W.
CORPORATE SOURCE: GraceCancer Drug Cent., Roswell Park Cancer Inst., Buffalo, NY, 14263, USA
SOURCE: Journal of Biological Chemistry (1993), 268(25), 19118-25
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
In MALME-3M human melanoma cells the polyamine analog N1,N12-bis(ethyl)spermine (BESPM) suppresses the key polyamine biosynthetic enzymes, ornithine and S-adenosylmethionine decarboxylase, and increases the polyamine-catabolizing enzyme, spermidine/spermine N1-acetyl-transferase (SSAT) by >200-fold. In the present study increases in SSAT activity in MALME-3M cells treated with 10 μM BESPM were accompanied by a substantial (≤45-fold) accumulation of SSAT mRNA. By Northern blot anal. 3 RNA transcripts were found to hybridize with the coding region of human SSAT cDNA: a minor high-mol.-weight (.apprx.3.5 kilobases) species designated form A and 2 lower-mol.-weight species designated forms B and C (.apprx.1.5 and .apprx.1.3 kilobases, resp.). Form A increased uniformly during BESPM treatment and was most obvious in nuclear RNA prepns. On the basis of size similarity to the transcribing region of the gene and hybridization with the coding region of SSAT cDNA and its prevalence in nuclear mRNA prepns., form A is thought to represent precursor SSAT RNA. Form C is present in control cells and increases steadily during treatment, whereas form B increases transiently during early treatment (1-3 h). By RNase H digestion assay, form B was found to have a 200-base pair longer poly(A) tract and as such may represent a precursor to form C. Accumulation of SSAT mRNA was a result of increased gene transcription and stabilization of SSAT mRNA. Nuclear run-on studies indicated a 2-4-fold increase in the transcription rate of the SSAT gene. As indicated by actinomycin D studies, the SSAT mRNA half-life increased with BESPM treatment from 17 to 64 h. The natural polyamine, spermine, also increased SSAT mRNA (5.5-fold at 24 h) and behaved similarly to BESPM in inducing the appearance of the same 3 transcript forms. The polyamine was much less effective than the analog at increasing enzyme activity. Lowering intracellular polyamine pools with inhibitors of biosynthesis decreased basal SSAT mRNA levels by at least 70% indicating, that the gene can be down-regulated as well as up-regulated by polyamines. Apparently, SSAT represents a unique example of gene expression being pos. influenced at the RNA level by polyamines and their analogs.

L6 ANSWER 67 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 50
ACCESSION NUMBER: 1994:210916 CAPLUS Full-text
DOCUMENT NUMBER: 120:210916
TITLE: Molecular mechanics calculations of the structures of polyamide nucleic acid DNA duplexes and triple helical hybrids
AUTHOR(S): Almarsson, Orn; Bruice, Thomas C.; Kerr, Janice; Zuckermann, Ronald N.
CORPORATE SOURCE: Dep. Chem., Univ. California, Santa Barbara, CA, 93106, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1993), 90(16), 7518-22
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English

ABSTRACT:
Polyamide nucleic acids (PNAs) have emerged as useful agents for recognition of single- and double-stranded nucleic acids. Interresidue hydrogen bonds between the amide carbonyl nearest the nucleobase and chain NH moieties provide inherent stability to the helical conformation of PNA 1. Moving the amide carbonyl away from the nucleobase to the backbone, and replacing it with a methylene group, results in 2 lacking the stabilizing hydrogen bond. Oligomers of 2 do not interact with DNA. Modeling suggests that 2 displays a more extended conformation than 1, and nucleobase orientation is disrupted in 2 in the absence of a cDNA strand. This is in contrast to 1, which retains a centrosym. arrangement of nucleobases. Structures for 1-T10.cntdot.DNA and (1-T10)2.cntdot.DNA species spanned by a pyrimidine strand (D-loop) were constructed. In the triple helical (1-T10)2.cntdot.DNA structure, the two PNA strands form the complementary Watson-Crick paired strand and the Hoogsteen base-paired strand in the major groove of the 1.cntdot.DNA duplex. The PNA strands are proposed to bind antiparallel to one another in (1-T10)2.cntdot.DNA structure. The factors suggested to account for the stability of this 2:1 complex are (i) a hydrophobic attraction between two PNA backbones and (ii) a favorable electrostatic effect resulting from replacement of a phosphodiester backbone by a neutral peptide backbone.

L6 ANSWER 68 OF 98 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN DUPLICATE 51
ACCESSION NUMBER: 1993:450223 BIOSIS Full-text
DOCUMENT NUMBER: PREV199396095123
TITLE: Microgonotropens and their interactions with DNA: 3. Structural analysis of the 1:1 complex of d(CGCAAATTTGCG)-2 and dien-microgonotropen c by 2D NMR spectroscopy and restrained molecular modeling.
AUTHOR(S): Blasko, Andrei; Browne, Kenneth A.; He, Gong-Xin; Bruice, Thomas C. [Reprint author]
CORPORATE SOURCE: Dep. Chem., Univ. Calif., Santa Barbara, CA 93106, USA
SOURCE: Journal of the American Chemical Society, (1993) Vol. 115, No. 16, pp. 7080-7092.
CODEN: JACSAT. ISSN: 0002-7863.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 5 Oct 1993
Last Updated on STN: 6 Oct 1993

ABSTRACT:
The solution structures of d(CGCAAATTTGCG)-2 and the 1:1 complex of d(CGCAAATTTGCG)-2 with dien-microgonotropen-c (Sc) have been determined by 1D and 2D 1H NMR spectroscopy and restrained molecular modeling. One hundred and two resonances for the free DNA and 196 for the ***DNA*** bound to Sc have been assigned. The 1D (DNA imino protons) and 2D (NOESY) spectra of the 1:1 complex show that there is an asymmetric type of binding in the A+T-rich region involving five base pairs (5'-A-6T-7T-8T-9G-10). The two most stable structures of the d(CGCAAATTTGCG)-2:Sc complex have (i) pyrrole rings A and B coplanar and in the minor groove with pyrrole ring C out of plane by apprx 70 degree and (ii) pyrrole rings A, B, and C coplanar and in the minor groove. The amino terminal acetamide head is directed toward A-6 while the carboxy terminal (dimethylamino)propyl tail is directed toward and above G-10. The energy barrier between the two bound Sc conformations is 2.5 kcal/mol in favor of the structure with only two pyrrole rings in the minor ***groove.*** The dien polyamino substituent residing on the nitrogen of pyrrole ring C runs above and along the phosphate backbone, toward the major ***groove.*** The protonated terminal dimethylamine nitrogen of the (dimethylamino)propyl tail is adjacent to a negatively charged phosphodiester-linkage (P-11) on the ***minor*** groove side, while the protonated dien nitrogens reside on the edge of the major groove and pair with the phosphodiester linkages P-8, P-9, and P-10. The off-rate of Sc from the 1:1 complex was found to be 1.3 +- 0.2 s-1, corresponding to an activation energy of 17 kcal/mol. The relative positions of the DNA proton signals change as Sc ***binds*** to the DNA. This is due, in part, to the widening of the minor groove (up to 3 ANG) in the binding site. Compound Sc binds 5-7 ANG from the bottom of the groove and 5-6 and 4-6 ANG distant from the (-) and (+) strands, respectively. Comparisons with the crystallographic data of the same DNA with and without distamycin were made. Molecular modeling of the free and Sc-bound DNA, based on NOE measurements, shows that there is a break in the C-2v symmetry of the crystallized DNA at the A-6T-7 junction as it goes into aqueous solution. An increase in the helical bend of 10.6 degree from that of the crystallized ***DNA*** was found to occur in the solution DNA while an increase of only 6.4 degree was found for the solution DNA:Sc complex relative to the crystallized dodecamer. Upon solvation, the length of the duplex increases by 0.1 ANG /bp for both the dodecamer and the Sc-complexed dodecamer compared to the case of crystal structures of free DNA and distamycin-complexed DNA.

L6 ANSWER 69 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 52
ACCESSION NUMBER: 1993:581208 CAPLUS Full-text
DOCUMENT NUMBER: 119:181208
TITLE: Chemistry of phosphodiesters, DNA and models. 3. Microgonotropens and their interactions with DNA. 1. Synthesis of the tripyrrole peptides dien-microgonotropen-a, -b, and -c and characterization of their interactions with dsDNA
AUTHOR(S): He, Gong Xin; Browne, Kenneth A.; Groppe, Jay C.; Blasko, Andrei; Mei, Houng Yau; Bruice, Thomas C.
CORPORATE SOURCE: Dep. Chem., Univ. California, Santa Barbara, CA, 93106, USA
SOURCE: Journal of the American Chemical Society (1993), 115(16), 7061-71
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 119:181208
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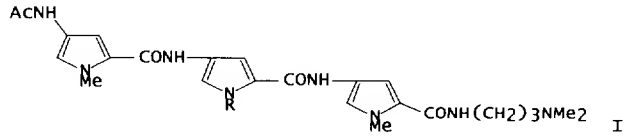

I

ABSTRACT:
Exploration of the novel idea of employing a pyrrole nitrogen of a tripyrrole peptide minor groove binding agent to carry catalytic entities to the phosphates and major groove to ***DNA*** has been initiated with the synthesis of dien-microgonotropen-a, -b, and -c [I; R = (CH2)nN(CH2CH2CH2NMe2)2, n = 3-5] (II). Replacing the carboxyl terminal amidine and amino terminal formyl functionalities of distamycin (Dm) by CH2NMe2 and Ac substituents, resp., provides I (R = Me), which has greater stability in water than does Dm. The synthetic design allows the N-Me substituent on the central pyrrole of I (R = Me) to be replaced by connectors terminating in a dien ligand (II). The binding of I (R = Me) is about 20-fold weaker than the binding of II to calf thymus ***DNA*** , poly(dA-dT), and poly(dI-dC) due to the contribution of the ***polyamine*** substituents of the latter. The specificity and affinity of ***binding*** of II to the 5'-[32P] 167-bp EcoRI/RsaI restriction fragment of pBR322 was determined by DNase I footprint anal. Specific inhibition of cleavage was observed at each of the four potential A+T-rich binding sites after preincubation with II at concns. as high as 50 μM. At 250 μM, binding at short heteropolymeric A+T secondary sites distal to the cluster of A+T-rich primary binding sites was observed At such higher concns. of II, increased rates of enzymic cleavage at specific sequences were observed DNase I footprinting anal. of the 3'-labeled fragment provided complementary results. Electrophoretic migration of HaeIII restriction digest fragments of φX-174-RF DNA after preincubation with II was used to assess induction of gross conformational changes in DNA mols. As the concentration of the agents increases, the effect of the agents in changing the conformation of larger DNA fragments decreases in the order II (n = 5) > II (n = 4) > II (n = 3) » Dm > Hoechst 33258. The electrophoretic mobilities of smaller DNA fragments are unaltered in the presence of the various agents. The dien-microgonotropens are much more effective in inducing changes than the sum of the Dm and bis[3-(dimethylamino)propyl]methylamine parts. This is due to the unique relationship between the minor ***groove*** binding portion of the dien-microgonotropens and the accompanying electrostatic complexing of the covalently attached dien moiety to the phosphodiester backbone of DNA.

L6 ANSWER 70 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1993:489820 CAPLUS Full-text
DOCUMENT NUMBER: 119:89820
TITLE: Enhanced ligation of DNA with a synthetic effector molecule
AUTHOR(S): Zuber, Guy; Sirlin, Claude; Behr, Jean Paul
CORPORATE SOURCE: Lab. Chim. Genet., Fac. Pharm., Illkirch, F67401, Fr.

SOURCE: Journal of the American Chemical Society (1993), 115(11), 4939-40
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
As a further step toward the long-term goal of designing enzyme mimics it is reported here that a spermine-histamine conjugate acts as a ligase substitute in enhancing the rate and yield of cyanoimidazole (cofactor)-promoted ligation of DNA. Indeed, it was previously shown that polyamines crawl along the DNA minor groove floor with little sequence selectivity. Thus spermine is an ideal vehicle to carry the potential acid/base catalyst imidazole in the neighborhood of the nick, where phosphate and hydroxyl ends are maintained close to each other by the intact strand. In the first set of expts. performed near room temperature (30°C) cyanoimidazole (ImCN) at 10 mM proved to be a poor ligating agent (15% after 18 h) even in the presence of Mg2+ (16%). However, addition of SperIm [spermine-5-(N-ethylimidazole)carboxamide, 0.1 mM] to the reaction mixture resulted in a substantial increase of ligated oligonucleotide (80%). Such an increase cannot be accounted for by the stabilizing effect of the spermine moiety on dangling reacting oligonucleotide ends (spermine actually decreases the yield to 10%) nor is it due solely to the presence of imidazole. Thus SperIm is unique in combining a DNA binding moiety with a putative catalyst. Next, for convenience, the time course of the reaction was followed at 4°C, where ImCN has extended lifetime (t1/2 = 72 h in 10 mM MES pH 6, as compared to 4 h at room temperature) and where the duplex is fully formed (Tm = 40°C). In the presence of SperIm (50 μM) the reaction progresses smoothly whereas ImCN (5 mM)/Mg2+ (10 mM) shows ligation that is hardly detectable. This experiment was repeated several times in order to approx. the kinetic enhancement factor. After a ca. 9-h lag time, the SperIm-enhanced reaction proceeds about 50-fold faster than the simple chemical ligation reaction.

L6 ANSWER 71 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 53
ACCESSION NUMBER: 1993:440309 CAPLUS Full-text
DOCUMENT NUMBER: 119:40309
TITLE: Inhibitors of human immunodeficiency virus integrase
AUTHOR(S): Fesen, Mark R.; Kohn, Kurt W.; Leteurtre, Francois; Pommier, Yves
CORPORATE SOURCE: Div. Cancer Treat., Natl. Cancer Inst., Bethesda, MD, 20892, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1993), 90(6), 2399-403
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
In an effort to further extend the number of targets for development of antiretroviral agents, we have used an in vitro integrase assay to investigate a variety of chems., including topoisomerase inhibitors, antimalarial agents, DNA binders, naphthoquinones, the flavone quercetin, and caffeic acid phenethyl ester as potential human immunodeficiency virus type 1 integrase inhibitors. Our results show that although several topoisomerase inhibitors-including doxorubicin, mitoxantrone, ellipticines, and quercetin-are potent integrase inhibitors, other topoisomerase inhibitors-such as amsacrine, etoposide, teniposide, and camptothecin-are inactive. Other intercalators, such as chloroquine and the bifunctional intercalator ditercalinium, are also active. However, DNA binding does not correlate closely with integrase inhibition. The intercalator 9-aminoacridine and the polyamine DNA minor-***groove*** binders spermine, spermidine, and distamycin have no effect, whereas the non-DNA binders primaquine, 5,8-dihydrox-1,4-naphthoquinone, and caffeic acid phenethyl ester ***inhibit*** the integrase. Caffeic acid phenethyl ester was the only compound that inhibited the integration step to a substantially greater degree than the initial cleavage step of the enzyme. A model of 5,8-dihydroxy-1,4-naphthoquinone interaction with the zinc finger region of the retroviral integrase protein is proposed.

L6 ANSWER 72 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 54
ACCESSION NUMBER: 1993:207741 CAPLUS Full-text
DOCUMENT NUMBER: 118:207741
TITLE: DNA unwinding upon strand-displacement binding of a thymine-substituted polyamide to double-stranded DNA
AUTHOR(S): Cherny, Dmitry Y.; Belotserkovskii, Boris P.; Frank-Kamenetskii, Maxim D.; Egholm, Michael; Buchardt, Ole; Berg, Rolf H.; Nielsen, Peter E.
CORPORATE SOURCE: Inst. Mol. Genet., Moscow, 123182, Russia
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1993), 90(5), 1667-70
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
It was recently found that polyamide nucleic acid (PNA) analogs consisting of thymines attached to an aminoethylglycine backbone bind strongly and sequence-selectively to adenine sequences of oligonucleotides and double-stranded DNA (Nielsen, P. E., et al., 1991). It was concluded that the binding to double-stranded DNA was accomplished via strand displacement, in which the PNA bound to the Watson-Crick complementary adenine-containing strand, whereas the thymine-containing strand was extruded in a virtually single-stranded conformation. This model may provide a general way in which to obtain sequence-specific recognition of any sequence in double-stranded DNA by Watson-Crick hydrogen-bonding base-***pair*** recognition, and it is thus paramount to rigorously establish this ***binding*** mode for synthetic DNA-binding ligands. Such results from electron microscopy are reported. Furthermore, it is shown that binding of PNA to closed circular DNA results in unwinding of the double helix corresponding to approx. one turn of the double helix per 10 base pairs. The DNA-PNA complex, which is formed at low salt concentration (only a small portion of DNA mols. show complex formation at NaCl concentration higher than 40 mM), is exceptionally kinetically stable and cannot be dissociated by increasing salt concentration up to 500 mM.

L6 ANSWER 73 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 55
ACCESSION NUMBER: 1993:207735 CAPLUS Full-text
DOCUMENT NUMBER: 118:207735
TITLE: Effects of polyamines on the binding of Hoechst 33258 to calf thymus DNA
AUTHOR(S): Snyder, Ronald D.
CORPORATE SOURCE: Marion Merrell Dow Res. Inst., Cincinnati, OH, 45215, USA
SOURCE: Nucleosides & Nucleotides (1993), 12(1), 31-7
CODEN: NUNUD5; ISSN: 0732-8311
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
The ability of polyamines to displace the minor ***groove*** -binding dye Hoechst 33258 from calf thymus DNA was investigated. Polyamines displace nonspecific DNA phosphate-bound Hoechst in a charge-dependent fashion, but show very little ability to displace the high affinity binding of Hoechst in the ***minor*** groove of DNA. This high affinity ***binding*** is, however, sensitive to ethidium bromide and the ***minor*** groove binding drug berenil. These studies suggest that polyamines probably bind DNA in the ***minor*** groove very weakly, if at all, relative to known ***minor*** groove binding agents.

L6 ANSWER 74 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 56
ACCESSION NUMBER: 1992:419902 CAPLUS Full-text
DOCUMENT NUMBER: 117:19902
TITLE: Rational design of substituted tripyrrole peptides that complex with DNA by both selective minor-groove binding and electrostatic interaction with the phosphate backbone
AUTHOR(S): Bruice, Thomas C.; Mei, Houng Yau; He, Gong Xin; Lopez, Van
CORPORATE SOURCE: Dep. Chem., Univ. California, Santa Barbara, CA, 93106, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1992), 89(5), 1700-4
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English
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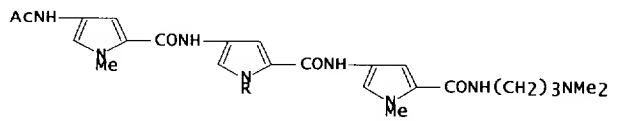

I, R=$(CH_2)_nN[(CH_2)_3NMe_2]_2$
II, R=Me

ABSTRACT:

The structures of the compds. (I, n = 3-5) that incorporate (i) the tripyrrole peptide of the minor-groove-binding distamycin class of compds. and (ii) polyamine ligands that extend from the ***minor*** groove and can interact with phosphodiester bonds-were arrived at by computer-graphics designing by using the x-ray structure of distamycin A complexed in the minor groove of d(CGCAAATTTGCG)2. I are elaborations of distamycin analog (II), designed for improved stability in solution and easier synthesis and purification, which itself ***binds*** weakly to DNA. I were synthesized, and the interaction of distamycin A, and I with calf thymus DNA, poly(dA-dT), poly(dG-dC), poly(dI-dC), pBR322 superhelical plasmid DNA were studied. Binding of I occurs in the minor groove of DNA and, because of favorable electrostatic interaction of diprotonated polyamine side chains and DNA phosphodiester linkages, the tenacity of DNA binding and site specificity of I are comparable to that of native distamycin A. I (n = 4) induced changes in the superhelical d. of pBR322 plasmid DNA. The study establishes that the central pyrrole NMe substituent of II can be replaced by bulky ***polyamine*** metal ligands to create any number of compds. that bind into the minor groove at A + T-rich sites and are putative catalysts for the hydrolysis of DNA.

L6 ANSWER 75 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 57
ACCESSION NUMBER: 1992:647274 CAPLUS Full-text
DOCUMENT NUMBER: 117:247274
TITLE: Survey of the DNA binding properties of natural and synthetic polyamino compounds
AUTHOR(S): Stewart, Kent D.; Gray, Thomas A.
CORPORATE SOURCE: Winship Cancer Cent., Emory Univ., Atlanta, GA, 30322, USA
SOURCE: Journal of Physical Organic Chemistry (1992), 5(8), 461-6
CODEN: JPOCEE; ISSN: 0894-3230
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Using a fluorescence-detected ethidium displacement assay, the calf thymus ***DNA*** complexation properties of 27 mono-, di-, tetra- and hexacationic ***polyamines*** were determined The DNA-binding activity of these polyamine compds. increased with increasing cationic charge on the polyamine. Although most of the compds. exhibited no ***base*** pair binding selectivity, two of the tricationic polyamines possessing addnl. neutral amine groups exhibited approx. ten-fold GC binding selectivities.

L6 ANSWER 76 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 58
ACCESSION NUMBER: 1991:201893 CAPLUS Full-text
DOCUMENT NUMBER: 114:201893
TITLE: Polyamine-induced B-DNA to Z-DNA conformational transition of a plasmid DNA with (dG-dC)n insert
AUTHOR(S): Thomas, T. J.; Gunnia, Uma B.; Thomas, Thresia
CORPORATE SOURCE: Robert Wood Johnson Med. Sch., Univ. Med. and Dent. New Jersey, New Brunswick, NJ, 08903, USA
SOURCE: Journal of Biological Chemistry (1991), 266(10), 6137-41
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
The ability of natural polyamines putrescine, spermidine, and spermine to provoke a left-handed Z-DNA conformation in a recombinant plasmid (pDHg16) with a 23-base pair insert of (dG-dC)n·(dG-dC)n sequences was investigated. A monoclonal anti-Z-***DNA*** antibody (Z22) and an ELISA protocol were used to show that spermidine and spermine were capable of converting pDHg16 to the Z-DNA form. The concns. of spermidine and spermine at the midpoint of the B-***DNA*** to Z-DNA transition were 280 and 5 μM, resp., in buffer containing 50 mM NaCl, 1 mM sodium cacodylate, and 0.15 mM EDTA, pH 7.4. A plot of ln[Na+] vs. in [spermine4+], where [Na+] is the bulk NaCl concentration and [spermine4+] is the spermine concentration at the midpoint of the B-DNA to Z-DNA transition, gave a straight line with a slope of 1.2. Structural specificity was clearly evident in the efficacy of 3 spermidine homologs to induce the Z-DNA conformation in pDHg16. Putrescine and acetylspermidines had no effect on the conformation of the plasmid DNA up to a 3 mM concentration Control expts. with the parental plasmid (pDL6) showed no ***binding*** of the plasmid DNA with Z22. These results indicate that spermidine and spermine are capable of provoking the left-handed Z-***DNA*** conformation in small blocks of (dG-dC)n sequences embedded in a right-handed B-DNA matrix. Since blocks of (dG-dC)n sequences are found in certain native DNAs, conformational alterations of these regions to the Z-DNA form in the presence of polyamines may have important gene regulatory effects.

L6 ANSWER 77 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 59
ACCESSION NUMBER: 1991:180517 CAPLUS Full-text
DOCUMENT NUMBER: 114:180517
TITLE: Location of spermine and other polyamines on DNA as revealed by photoaffinity cleavage with poly(amino)benzenediazonium salts
AUTHOR(S): Schmid, Nathalie; Behr, Jean Paul
CORPORATE SOURCE: Fac. Pharm., Strasbourg, 67401, Fr.
SOURCE: Biochemistry (1991), 30(17), 4357-61
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Although polyamines interact strongly with nucleic acids, x-ray and NMR studies have revealed only a little structural information about spermine-***DNA*** complexes. Therefore, it was of interest to look at the ***binding*** of polyamines to 32P-labeled DNA restriction fragments by sequencing gel electrophoresis of the photoaffinity cleavage products induced by polyaminobenzenediazonium salts. The shift of cleavage patterns observed on opposite strands as well as competition expts. with distamycin shows polyamines to be located in the ***minor*** groove of B-DNA and to depend on the nucleic acid polymorphism, jumping to the major groove in the A-form. The sequence selectivities of various polycations (spermine, putrescine, and cobalt(III) hexaammine) are similar and slightly favor A,T-rich regions. Taken together, these results show that polycations which are not point charges are guided by the electroneg. potential along the nucleic acid and suggest fast crawling of the polyamine within the minor ***groove*** , due to individual NH2+ jumping between multiple equidistant and isoenergetic bidentate hydrogen-bonding sites. Such a picture could be the clue to the NMR and frequently silent x-ray behavior of polyamines when bound to DNA.

L6 ANSWER 78 OF 98 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 91:267192 SCISEARCH Full-text
THE GENUINE ARTICLE: FK234
TITLE: LOCATION OF SPERMINE AND OTHER POLYAMINES ON DNA AS REVEALED BY PHOTOAFFINITY CLEAVAGE WITH POLYAMINOBENZENEDIAZONIUM SALTS
AUTHOR: SCHMID N; BEHR J P (Reprint)
CORPORATE SOURCE: FAC PHARM STRASBOURG, CNRS, URA 1386, F-67401 STRASBOURG, FRANCE
COUNTRY OF AUTHOR: FRANCE
SOURCE: BIOCHEMISTRY, (1991) Vol. 30, No. 17, pp. 4357-4361.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 38
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
ABSTRACT:
Although polyamines interact strongly with nucleic acids, X-ray and NMR studies have not revealed much structural information about spermine-***DNA*** complexes. Therefore, it was of interest to look at the ***binding*** of polyamines to P-32-labeled DNA restriction fragments by sequencing gel electrophoresis of the photoaffinity cleavage products induced by polyaminobenzenediazonium salts. The shift of cleavage patterns observed on opposite strands as well as competition experiments with distamycin shows polyamines to be located in the ***minor*** groove of B-DNA and to depend on the nucleic acid polymorphism, jumping to the major groove in the A-form. The sequence selectivities of various polycations (spermine, putrescine, and cobalt(III) hexaammine) are similar and slightly favor A,T-rich regions. Taken together, these results show that polycations which are not point charges are guided by the electronegative potential along the nucleic acid and suggest fast crawling of the polyamine within the ***minor*** groove, due to individual NH2+ jumping between multiple equidistant and isoenergetic bidentate hydrogen-bonding sites. Such a picture could be the clue to the unexpected NMR and to the frequently silent X-ray behavior of polyamines when bound to DNA.

L6 ANSWER 79 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1991:181471 CAPLUS Full-text
DOCUMENT NUMBER: 114:181471
TITLE: Two new photoaffinity polyamines appear to alter the helical twist of DNA in nucleosome core particles
AUTHOR(S): Clark, Elizabeth; Swank, Richard A.; Morgan, James E.; Basu, Hirak; Matthews, Harry R.
CORPORATE SOURCE: Dep. Biol. Chem., Univ. California, Davis, CA, 95616, USA
SOURCE: Biochemistry (1991), 30(16), 4009-20
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English

ABSTRACT:
Two new photoaffinity derivs. of polyamines have been synthesized by the reaction of spermine or spermidine with Me 4-azidobenzimidate. The new compds. were purified chromatog. and characterized by several methods including proton magnetic resonance spectroscopy. The spermine derivative is N1-ABA-spermine [(azidobenzamidino)spermine], and the spermidine derivative is a mixture of N1- and N8-ABA-spermidine. ABA-spermine stabilizes nucleosome core particles in thermal denaturation expts., with similar but not identical effects when compared with the parent polyamine, spermine. In CD expts., ABA-spermine was capable of producing a B → Z transition in poly(dG-m5dC) at a concentration of 30 μM, compared with 5 μM required to produce the same effect with spermine. On the other hand, ANB-spermine [(azidonitrobenzoyl)spermine; Morgan, J. E., et al. stabilized the B form of poly(dG-br5dC). ABA-spermine is a potent inhibitor of ornithine decarboxylase from Escherichia coli, giving 50% inhibition at 0.12 mM, while ANB-spermine is a modest inhibitor, comparable to spermine or spermidine. Under conditions of nitrogen-limited growth, yeast take up ABA-spermine and ABA-spermidine at approx. one-third to one-half the rate of spermidine or spermine. In contrast, ANB-spermine was not significantly taken up. The photoaffinity polyamines were used to photoaffinity label the DNA in nucleosome core particles, and the sites of labeling were determined by exonuclease protection. All photoaffinity reagents showed both nonspecific labeling and specific sites of higher occupancy. However, the positions of the sites varied: the ANB-spermine sites confirmed those previously reported (Morgan et al., 1980); the ABA-spermine and ABA-spermidine sites were spaced at 9.8 base pair intervals from the 3' end of each DNA strand. This observation, together with the effect of spermine on the CD of DNA in nucleosome core particles, implies that polyamines alter the helical twist of DNA in nucleosome core particles. The ABA-polyamines are offered as general-purpose photoaffinity polyamine reagents.

L6 ANSWER 80 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 60
ACCESSION NUMBER: 1991:77184 CAPLUS Full-text
DOCUMENT NUMBER: 114:77184
TITLE: Kinetic and equilibrium analysis of a threading intercalation mode: DNA sequence and ion effects
AUTHOR(S): Tanious, Farial A.; Yen, Shau Fong; Wilson, W. David
CORPORATE SOURCE: Dep. Chem., Georgia State Univ., Atlanta, GA, 30303, USA
SOURCE: Biochemistry (1991), 30(7), 1813-19
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
The interaction of a sym. naphthalene diimide with alkylamino substituents at each imide position was investigated with the alternating sequence polymers, poly[d(A-T)]2 and poly[d(G-C)]2. Spectrophotometric ***binding*** studies indicated strong binding of the diimide to both sequences, although the guanine-cytosine binding constant was 20-25-fold larger than the adenine-thymine binding constant Anal. of the effects of salt concentration on the binding equilibrium showed that the diimide forms 2 ion pairs in its complex with both polymers, as expected for a simple dication. Stopped-flow kinetics expts. demonstrated that the diimide both assocs. and dissocs. from DNA more slowly than classical ***intercalators*** with similar binding consts. Anal. of salt concentration effects on dissociation kinetics rate consts. (kd) revealed that slopes in log kd vs. log[Na+] plots were only .apprx.50% of the value obtained for classical dicationic intercalators that have both charged groups in the same groove. These kinetic results supported a threading ***intercalation*** model, with 1 charged diimide substituent in each of the ***DNA*** grooves rather than with both side-chains in the same groove, for the diimide complex with DNA. In the rate-determining step of the mechanism for dissociation of a threading complex, only 1 ion pair was broken; the free side-chain could then slide between these base pairs to put both diimide side-chains in the same groove, and this wass followed by rapid full dissociation of the diimide. This sequential release of ion pairs made the dissociation slope for dicationic threading intercalators more similar to the slope for classical monocationic intercalating ligands. Kinetic studies, thus, provide a very clear method for distinguishing classical from threading intercalators. Similar expts. can also distinguish intercalation from groove-binding modes.

L6 ANSWER 81 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 61
ACCESSION NUMBER: 1990:131987 CAPLUS Full-text
DOCUMENT NUMBER: 112:131987
TITLE: Effect of ionic strength and cationic DNA affinity binders on the DNA sequence selective alkylation of guanine N7-positions by nitrogen mustards
AUTHOR(S): Hartley, John A.; Forrow, Stephen M.; Souhami, Robert L.
CORPORATE SOURCE: Dep. Oncol., Univ. Coll., London, W1P 8BT, UK
SOURCE: Biochemistry (1990), 29(12), 2985-91
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Large variations in alkylation intensities exist among guanines in a ***DNA*** sequence following treatment with chemotherapeutic alkylating agents such as nitrogen mustards, and the substituent attached to the reactive group can impose a distinct sequence preference for reaction. In order to understand further the structural and electrostatic factors which determine the sequence selectivity of alkylation reactions, the effect of increased ionic strength, the intercalator ethidium bromide, AT-specific ***minor*** groove binders distamycin A and netropsin, and the polyamine spermine on guanine N7-alkylation by L-phenylalanine mustard (L-Pam), uracil mustard (UM), and quinacrine mustard (QM) was investigated with a modification of the guanine-specific chemical cleavage technique for DNA sequencing. For L-Pam and UM, increased ionic strength and the cationic DNA affinity binders dose dependently inhibited the alkylation. QM alkylation was less ***inhibited*** by salt (100 mM NaCl), ethidium (10 μM), and spermine (10 μM). Distamycin A and netropsin (100 μM) gave and enhancement of overall QM alkylation. More interestingly, the pattern of guanine N7-alkylation was qual. altered by ethidium bromide, distamycin A, and netropsin. The result differed with both the nitrogen mustard (L-Pa < UM < QM) and the cationic agent used. The effect, which resulted in both enhancement and suppression of alkylation sites, was most striking in the case of netropsin and distamycin A, which differed from each other. DNA footprinting indicated that selective binding to AT sequences in the minor ***groove*** of DNA can have long-range effects on the alkylation pattern of DNA in the major groove.

L6 ANSWER 82 OF 98 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN DUPLICATE 62
ACCESSION NUMBER: 1990:175623 BIOSIS Full-text
DOCUMENT NUMBER: PREV199089092793; BA89:92793
TITLE: INTERACTION OF ENHANCER-BINDING PROTEIN EBP1 NF-KAPPA-B WITH THE HUMAN IMMUNODEFICIENCY VIRUS TYPE 1 ENHANCER.
AUTHOR(S): CLARK L [Reprint author]; MATTHEWS J R; HAY R T
CORPORATE SOURCE: DEP BIOCHEM MICROBIOL, UNIV ST ANDREWS, FIFE, KY16 9AL SCOTLAND, UK
SOURCE: Journal of Virology, (1990) Vol. 64, No. 3, pp. 1335-1344. CODEN: JOVIAM. ISSN: 0022-538X.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 10 Apr 1990
Last Updated on STN: 10 Apr 1990
ABSTRACT:
Human EBP1, isolated from HeLa cells, binds to a 10-base-***pair*** (bp) sequence in cellular and viral enhancers that is also recognized by the inducible transcription factor NF-κB.
Here we describe the interaction of purified EBP1 with the 10-bp repeated sequence that is responsive to signals which activate T cells and which form part of the human immunodeficiency virus type 1 (HIV-1) enhancer.
DNase I footprinting indicates that both 10-bp sites on the same molecule, located between -80 and -105 on the HIV-1 long terminal repeat, can be occupied by EBP1, while dimethyl sulfate protection and methylation interference experiments indicate which purine bases are in contact with the protein.
The presence of bases which exhibit increased rates of dimethyl sulfate-induced methylation in the presence of EBP1 indicate that interaction of EBP1 with its recognition site is accompained by distortion of the DNA double helix.
Supporting this conclusion is the observation that the polyamine spermidine dramatically increases EBP1 binding to its cognate site on the DNA.
Studies with human T cells (Jurkat) and nucleotide stimulation data suggest that EBP1 is the activated form of NF-κB in these cells.

L6 ANSWER 83 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 63
ACCESSION NUMBER: 1990:526049 CAPLUS Full-text
DOCUMENT NUMBER: 113:126049
TITLE: Kinetics of the binding of mitoxantrone, ametantrone and analogs to DNA: relationship with binding mode and antitumor activity
AUTHOR(S): Denny, W. A.; Wakelin, L. P. G.
CORPORATE SOURCE: Sch. Med., Univ. Auckland, Auckland, N. Z.
SOURCE: Anti-Cancer Drug Design (1990), 5(2), 189-200
CODEN: ACDDEA; ISSN: 0266-9536
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
The kinetics of association and dissociation of DNA complexes of the antitumor agents mitoxantrone, ametantrone and related 1,4-bis(***alkylamino***)anthraquinones have been determined by stopped-flow

spectrophotometry, in order to study relationships between structure, kinetic parameters and biol. activity. Variations in the structure of the side chains of ametantrone analogs had little effect on the kinetic stability of the complexes, but the mitoxantrone complexes dissociated about an order of magnitude more slowly, suggesting an important role for the two hydroxyl groups on the chromophore of the latter compound The results are consistent with other NMR and mol. mechanics data, which suggest a binding model where the chromophore intercalates perpendicularly to the DNA ***base*** pair axis. Dissociation studies with DNA homopolymers of varying base composition suggest the kinetic mechanism is a mixed parallel/sequential one, with the slowest dissociation processes being from GC-rich sites in both homopolymers and natural DNA. The results suggest guidelines for the design of more tumor-active analogs of the class.

L6 ANSWER 84 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 64

ACCESSION NUMBER: 1989:610787 CAPLUS Full-text
DOCUMENT NUMBER: 111:210787
TITLE: Molecular dynamics of spermine-DNA interactions: sequence specificity and DNA bending for a simple ligand
AUTHOR(S): Feuerstein, Burt G.; Pattabiraman, Nagarajan; Marton, Laurence J.
CORPORATE SOURCE: Sch. Med., Univ. California, San Francisco, CA, 94143, USA
SOURCE: Nucleic Acids Research (1989), 17(17), 6883-92
CODEN: NARHAD; ISSN: 0305-1048
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Mol. dynamics was used to model interactions between the physiol. important ***polyamine*** spermine and 2 B-DNA oligomers, the homopolymer (dG)10-(dC)10 and the heteropolymer (dGdC)5-(dGdC)5. Water and counterions were included in the simulation. Starting coordinates for the spermine-***DNA*** complexes were structures obtained by mol. mechanism modeling of spermine with the 2 oligomers; in these models, spermine binding induced a bend in the heteropolymer but not in the homopolymer. During .apprx.40 psec of mol. dynamics simulation, spermine moves away from the floor of the major groove and interacts nonspecifically with d(G)10-d(C)10. In contrast, a spermine-induced bend in the helix of (dGdC)5-(dGdC)5 is maintained throughout the simulation and spermine remains closely associated with the major groove. These results provide further evidence that the binding of spermine to nucleic acids can be sequence specific and that bending of alternating purine-pyrimidine sequences may be a physiol. important result of spermine ***binding.***

L6 ANSWER 85 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1990:490927 CAPLUS Full-text
DOCUMENT NUMBER: 113:90927
TITLE: Molecular basis for potentiation of bleomycin-mediated degradation of DNA by polyamines. Experimental and molecular mechanical studies
AUTHOR(S): Strekowski, Lucjan; Harden, Donald B.; Wydra, Roman L.; Stewart, Kent D.; Wilson, W. David
CORPORATE SOURCE: Dep. Chem., Georgia State Univ., Atlanta, GA, 30303, USA
SOURCE: Journal of Molecular Recognition (1989), 2(4), 158-66
CODEN: JMORE4; ISSN: 0952-3499
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
The bleomycin-mediated degradation of DNA is stimulated (amplified) by certain DNA binding compds., such as polyamines, that distort the double helix. Computer modeling studies suggest that putrescine (1), spermidine (2), and spermine (3) bind preferentially on the floor of the major groove of (dGdC)5·(dGdC)5. This interaction results in a bend of the oligomer helix toward the ***major*** groove and enlargement of the minor ***groove*** , both effects being in the order 1 < 2 < 3. These ***polyamine*** -induced distortions, as obtained from theor. studies, parallel the exptl. values of the amplification activities of 1-3 in the bleomycin-mediated degradation of poly(dGdC)·poly(dGdC). The amplification mechanism of non-competitive binding of amplifier mols. in the ***major*** groove, and bleomycin in the minor ***groove*** , is proposed. It is suggested that the amplifier-induced conformational changes of the DNA helix increase affinity of the activated bleomycin complex toward the DNA minor ***groove*** and, consequently, result in an increased efficiency of the bleomycin-mediated degradation of the helix.

L6 ANSWER 86 OF 98 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 1988:196058 BIOSIS Full-text
DOCUMENT NUMBER: PREV198885097404; BA85:97404
TITLE: PROTON NMR STUDY OF THE BASE-PAIRING REACTIONS OF D-GGAATTCC SALT AND POLYAMINE EFFECTS OF THE IMINO PROTON EXCHANGE.
AUTHOR(S): BRAUNLIN W H [Reprint author]; BLOOMFIELD V A
CORPORATE SOURCE: DEP BIOCHEM, UNIV MINN, ST PAUL, MN 55108, USA
SOURCE: Biochemistry, (1988) Vol. 27, No. 4, pp. 1184-1191.
CODEN: BICHAW. ISSN: 0006-2960.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 21 Apr 1988
Last Updated on STN: 21 Apr 1988
ABSTRACT:
Salts and polyamines have a variety of effects on the physical properties of DNA, including stabilization against thermal melting. We wished to gain greater insight into the mechanism of this stabilization by ascertaining its effect on the dynamics of base opening and closing reactions, as measured by NMR.
Since the binding of spermidine(3+) is influenced by salt, and since spermidine may act as a base catalyst in proton exchange reactions, we have undertaken a study of salt and base catalyst effects on the imino proton exchange kinetics of a model oligomeric DNA.
The selective longitudinal NMR relaxation rates of the hydrogen-bonded imino protons of the self-complementary octadeoxyribonucleotide d(GGAATTCC) monitor the rate of the base-catalyzed chemical exchange of these protons with solvent water.
The exchange rates thus obtained provide a sensitive measure of the ***base*** -pair opening reactions of the DNA duplex.
Under conditions of low pH and no added base catalyst, the NMR relaxation rates allow the determination of kd, the rate constant for the dissociation of the octameric duplex into single strands.
Titration with the base catalyst tris(hydroxymethyl)aminomethane allows the determination of kop, the rate constant for the localized opening of individual ***base*** pairs, prior to dissociation.
A significant Na+ concentration dependence is found for kd.
From an analysis of this dependence, it is determined that 0.6 ± 0.1 sodium ion is released during the dissociation event.
The activation energy for helix dissociation (200 ± 5 kJ/mol) is not dependent on the sodium ion concentration, indicating that the dissociation is entropically driven by the release of bound sodium ions.
In agreement with previous results, no measurable salt dependence is found for kop, which is equal to about 100 s-1 at 25°C.
Under low-salt conditions, the trivalent cation spermidine decreases the rate of helix dissociation, again without affecting the activation energy for this process.
Diprotonated spermidine(2+) acts as an extremely effective catalyst of imino proton exchange.

L6 ANSWER 87 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 65

ACCESSION NUMBER: 1989:71469 CAPLUS Full-text
DOCUMENT NUMBER: 110:71469
TITLE: Recognition of Z-RNA and Z-DNA determinants by polyamines in solution: experimental and theoretical studies
AUTHOR(S): Basu, Hirak S.; Feuerstein, Burt G.; Zarling, David A.; Shafer, Richard H.; Marton, Laurence J.
CORPORATE SOURCE: Sch. Med., Univ. California, San Francisco, CA, 94143, USA
SOURCE: Journal of Biomolecular Structure & Dynamics (1988), 6(2), 299-309
CODEN: JBSDD6; ISSN: 0739-1102
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Protonated polyamines are among the most efficient cations that induce the left-handed Z-form in certain polynucleotides. It is not known, however, whether these cations bind to specific sites on Z-sequences in solution Potential polyamine binding sites were studied by measuring the effects of polyamines on the binding of purified IgGs to different regions of the Z-helix and by mol. mechanics modeling. The specific binding of anti-Z-DNA and anti-Z-***RNA*** IgGs to Z-helixes was studied as a function of spermidine or spermine concentration The effect of polyamines on the antibody-nucleic acid interaction was different for IgGs with different specificities for various determinants on the Z-helix. Polyamines inhibit the binding of certain anti-Z IgGs directed against specific sites probably at or near the interface between the major convex surface and the phosphate backbone, most likely by competing with the antibody binding site(s). In contrast, polyamines have no effect on other anti-Z IgGs directed against sites determined by the phosphate backbone. Furthermore, these cations can enhance the binding of anti-Z IgG directed against bulky groups at the C-5 position on the major convex surface of the helix; the enhancement may be related to charge neutralization. These data suggest the existence of a specific binding site(s) for polyamines on

both Z-DNA and Z-RNA in solution These binding sites have some similarity to those observed in oligonucleotide crystals. The exptl. evidence for specific spermine binding sites on the helical surface was supported by mol. mechanics modeling of the interaction of spermine with the major groove of (dG-dC)5·(dG-dC)5 in both the Z- and B-forms. The crystal coordinates of spermine-containing oligonucleotides in both the B- and Z-forms were used as the starting points for modeling studies. The potential energy of spermine bound to the major convex surface of the Z-form was much less favorable than that of spermine bound to the major groove of the B-form. In the presence of Na+, however, the Z-form-spermine complexes were favored over the B-form. Thus, both theor. and exptl. studies indicate that polyamines can specifically recognize Z-helical determinants in solution as well as in crystals.

L6 ANSWER 88 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1988:51439 CAPLUS Full-text
DOCUMENT NUMBER: 108:51439
TITLE: Polyamine-DNA interactions. Condensation of chromatin and naked DNA
AUTHOR(S): Smirnov, I. V.; Dimitrov, S.; Makarov, V. L.
CORPORATE SOURCE: Inst. Mol. Biol., Moscow, USSR
SOURCE: Molekulyarnaya Biologiya (Moscow) (1987), 21(5), 1411-21
CODEN: MOBIBO; ISSN: 0026-8984
DOCUMENT TYPE: Journal
LANGUAGE: Russian
ABSTRACT:
Flow linear dichroism (LD) and light scattering at 90° was used to study the condensation of both DNA and calf thymus chromatin induced by spermine, triamines NH3+(CH2)iNH+(CH2)jNH3+, where i, j: 3, 4 (spermidine), 3, 3, 2, 3, 2, 2, the diamines putrescine and cadaverine, and MgCl2. The different polyamines affected DNA and chromatin in a similar way. The degree of compaction of the chromatin fibers induced by spermine, triamines except 2, 2, and Mg2+ was identical. The triamine 2, 2 and the diamines studied do not condense either chromatin or DNA. Such a big difference in the action of the triamines indicates that not only the charge, but also the structure of the polycations are important for their interactions with DNA and chromatin. The stoichiometry of ***polyamine*** binding to chromatin at which condensation occurred is 2 polyamine mols. per DNA helical turn. ***Polyamines*** are presumed to bind to the exposed sites of core ***DNA*** every 10 base pairs. The extent of DNA phosphate neutralization by the histones is estimated to be .apprx.55%. A mixture of mono- and multivalent cations affected DNA and chromatin condensation competitively and not synergistically, as claimed in a recent report by D. Sen and D. M. Crothers (1986).

L6 ANSWER 89 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 66
ACCESSION NUMBER: 1986:142219 CAPLUS Full-text
DOCUMENT NUMBER: 104:142219
TITLE: Influence of DNA-binding drugs on chromatin condensation
AUTHOR(S): Sen, Dipankar; Crothers, Donald M.
CORPORATE SOURCE: Dep. Chem., Yale Univ., New Haven, CT, 06511, USA
SOURCE: Biochemistry (1986), 25(7), 1503-9
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Transient-elec. dichroism was used to study the ability of DNA-***binding*** drugs to affect the folding of chromatin from the 10- to the 30-nm fiber, either by themselves or in conjunction with multivalent cations. Variables considered include the cationic charge of the drug, the comparative influence of intercalation and groove binding as modes of interaction, and the effect of bisintercalation compared to monointercalation. A drug must have a charge of 3+ or greater in order to condense chromatin at concns. substantially lower than the concentration of chromatin, measured in ***base*** pairs. Drugs of low charge, whether groove ***binders*** or mono- or bisintercalators, are unable to condense chromatin on their own. Bisintercalators of high charge, however, are extremely efficient condensers, being able to cross-link chromatin with greater efficiency than polyamines of corresponding charge. When Mg2+ is used in combination with bisintercalators of high charge, the order of addition of the 2 dets. whether compaction or cross-linking is favored. Finally, the antibiotics actinomycin D [50-76-0], daunomycin [20830-81-3], and distamycin [39389-47-4], despite varied modes of binding to DNA, all ***inhibit*** the compaction of chromatin beyond a critical point in a remarkably similar manner.

L6 ANSWER 90 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1985:589197 CAPLUS Full-text
DOCUMENT NUMBER: 103:189197
TITLE: Quantitative correlations of biological activities of dactinomycin analogs and methotrexate derivatives with van der Waals volume
AUTHOR(S): Prabhakar, Y. S.; Handa, A.; Gupta, S. P.
CORPORATE SOURCE: Birla Inst. Technol. Sci., Pilani, 333031, India
SOURCE: Arzneimittel-Forschung (1985), 35(7), 1030-3
CODEN: ARZNAD; ISSN: 0004-4172
DOCUMENT TYPE: Journal
LANGUAGE: English
GRAPHIC IMAGE:

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

ABSTRACT:
The biol. activities, namely the ability to bind with DNA ***base*** pairs and the in vitro inhibition of human lymphoblastic leukemia cells of certain C-7- and N2-substituted dactinomycin (actinomycin D, AMD) analogs I (R1 = H, OH, alkoxy, etc.; R2 = NH2, ***alkylamine***), and the growth inhibitory activity of a series of side chain substituted methotrexate (MTX) derivs. II (R = R1 = NH, OH, alkoxy, alkylamine, amine, etc.) and III (R = H, alkyl, etc.) against L 1210 mouse leukemia cells in culture and their binding affinity for dihydrofolate reductase (DHFR) [9002-03-3] enzyme extracted from this system and L. casei were significantly correlated with van der Waals volume of the substituents. In case of MTX derivs., not only the side chain substituted analogs but certain ring substituted analogs, too had their different activities dependent upon the van der Waals volume of the substituents. In case of side chain substituted analogs, however, the size of the substituent of α-position produced a greater effect on the activity than that of γ-position. Based on the correlating equations obtained, the drug-receptor interaction might involve either hydrophobic interaction or the van der Waals type of interaction.

L6 ANSWER 91 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 67
ACCESSION NUMBER: 1985:484702 CAPLUS Full-text
DOCUMENT NUMBER: 103:84702
TITLE: Isolation and characterization of small heat-stable acid-soluble DNA-binding proteins from Bacillus subtilis nucleoids
AUTHOR(S): Salti, V.; Le Hegarat, F.; Hirschbein, L.
CORPORATE SOURCE: Inst. Microbiol., Univ. Paris-Sud, Orsay, 91405, Fr.
SOURCE: Journal of General Microbiology (1985), 131(3), 581-90
CODEN: JGMIAN; ISSN: 0022-1287
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Small heat-stable, acid-soluble proteins (HASP) were isolated from B. subtilis nucleoids obtained from cell lysates of low ionic strength and lysozyme concentration They were identified by their ability to bind homologous and heterologous native and denatured DNA. Four major species, of 8.5, 12, 23, and 26 kilodalton (kDa), were found. Their affinity for DNA was moderate as measured by the sensitivity to ionic strength of the ***DNA*** -protein complex (0.1-0.4M NaCl). Partial digestion by micrococcal nuclease of the "low ionic strength nucleoids" released a DNA fragment of 80-120 base pairs. The data reported here indicate that small basic proteins, together with other components such as ***RNA*** , cations, and polyamines, may be involved in the compaction of the prokaryotic genome.

L6 ANSWER 92 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 68
ACCESSION NUMBER: 1983:535702 CAPLUS Full-text
DOCUMENT NUMBER: 99:135702
TITLE: Acridine-psoralen amines and their interaction with deoxyribonucleic acid
AUTHOR(S): Hansen, John Bondo; Koch, Torben; Buchardt, Ole; Nielsen, Peter E.; Wirth, Michael; Norden, Bengt
CORPORATE SOURCE: Chem. Lab. II, Univ. Copenhagen, Copenhagen, Den.
SOURCE: Biochemistry (1983), 22(21), 4878-86
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
A series of novel compds. in which a 9-acridinyl nucleus is linked to a psoralen nucleus in the 5- or 8-position via polyamines were prepared and examined Their reversible and irreversible binding to DNA and DNA crosslinking on irradiation with UV light (320-390 nm) were examined These compds. were all less efficiently photoreactive than 8-methoxypsoralen (I), both in crosslinking and photobinding to DNA, whereas the ratio between their photobinding and crosslinking was 40- to 400-fold that of I. Compds. in which the linker was attached to the 5-position

in psoralen showed smaller crosslinking and photobinding efficiencies and larger ratios between photobinding and crosslinking than those of psoralens attached in the 8-position. This strongly indicates that the 9-substituents of the acridines are oriented toward the minor groove. Flow linear dichroism studies showed that the compds. were DNA-***intercalating*** with the acridine moiety, whereas the psoralen moiety in no case was clearly intercalating. This conclusion was further supported by viscometry studies which also strongly indicated monointercalation.

L6 ANSWER 93 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1981:599475 CAPLUS Full-text
DOCUMENT NUMBER: 95:199475
TITLE: Accessibility of metaphase chromosomes from Chinese hamster ovary cells to DNase II
AUTHOR(S): Fittler, F.; Ibel, K.; Hoerz, W.
CORPORATE SOURCE: Inst. Physiol. Chem. Phys. Biochem. Zellbiol., Univ. Munich, Munich, 8000/2, Fed. Rep. Ger.
SOURCE: FEBS Letters (1981), 132(2), 341-3
CODEN: FEBLAL; ISSN: 0014-5793
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Metaphase chromosome structure in polyamine (spermine or spermidine)-containing buffer as compared to that in control (Tris-Ca2+) buffer showed structural alterations as evidenced by DNase II cleavage patterns. Digestion of chromosomes treated with polyamines indicated decreased ***DNA*** accessibility in these prepns. as compared to the control [.apprx.90 base-pair (bp) periodicity vs. .apprx.177 bp periodicity, resp.], and microscopic studies indicated a smaller diameter for the treated preparation The decreased accessibility of DNA reflects a higher compaction and more condensed state of DNA in the metaphase chromosome. The polyamine effect, due to a tighter binding to chromatin as compared to Ca2+ binding, evidently alters (compacts) chromatin structure. The exact mode of polyamine action is not known.

L6 ANSWER 94 OF 98 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1981:229504 BIOSIS Full-text
DOCUMENT NUMBER: PREV198172014488; BA72:14488
TITLE: CATION INDUCED TOROIDAL CONDENSATION OF DNA STUDIES WITH HEXAMINE COBALT III.
AUTHOR(S): WIDOM J [Reprint author]; BALDWIN R L
CORPORATE SOURCE: DEP BIOCHEM, SCH MED, STANFORD UNIV, STANFORD, CALIF 94305, USA
SOURCE: Journal of Molecular Biology, (1980) Vol. 144, No. 4, pp. 431-454.
CODEN: JMOBAK. ISSN: 0022-2836.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ABSTRACT:
The polyamines spermidine (3+) and spermine (4+) cause a cooperative intramolecular condensation of T7 or λ phage DNAs in which the ***DNA*** assumes a compact toroidal conformation.
An inert trivalent metal ion complex, Co3+ (NH3)6, also causes [yeast] ***DNA*** condensation, and DNA condensation in aqueous solution is caused by cations of charge 3+ or more.
The DNA products of polyamine-induced and of cobalt hexamine-induced condensation have similar toroidal conformations as judged by EM and both have the circular dichroism spectrum of DNA B-form, in contrast to the ψ
DNA condensates studied by Maniatis et al. (1974).
Monovalent and divalent cations (Na+, Mg2+) reverse DNA condensation.
Competition between inducing (3+ or 4+) and reversing (1+ or 2+) cations follows the ion-exchange behavior outlined in Manning's theory of atmospheric cation binding to DNA.
DNA condensation can apparently occur when a critical fraction of the ***DNA*** phosphate charge has been neutralized by cations adsorbed to the ***DNA.***
Cation-induced DNA condensation in aqueous solution may result from cation crosslinking:electrostatic bridging of adjacent helices by trivalent or higher valence cations.
Transition curves for DNA condensation were measured by the increase in light-scattering, using a photon-counting fluorimeter.
To ensure that equilibrium is reached, condensation was studied in both the forward the reverse directions, by using either Na+ or Mg2+ to reverse the reaction.
The kinetics of condensation are slow in the forward direction, in the time range of min to h, and slow as the DNA concentration is increased.
Reversal of condensation by Na+ or Mg2+ occurs more rapidly, in s to min, and the transition midpoints are essentially independent of DNA concentration.
At DNA concentrations below 1 μM-phosphate, the kinetics of condensation and of de-condensation are comparable in rate.
Intermolecular DNA contacts may compete with, and slow down, intramolecular condensation. equilibrium data for transition midpoints are obtained in either the forward or reverse direction at sufficiently low ***DNA*** concentrations; at higher DNA concentrations, equilibrium is reached in the reverse but not in the forward direction.
Phase diagrams for condensation (plots of log [Co3+ (NH3)6] vs. log [Na+] or log [Mg2+] at the transition midpoint) have been obtained from studies of de-condensation by Na+ or Mg2+.
These plots have a slope of +1 when either Co3+ (NH3)6, spermidine (3+) or spermine (4+) is used to induce condensation.
As shown by Wilson and Bloomfield, a slope of +1 is consistent with DNA condensation occurring when a critical fraction of DNA charge has been neutralized, as calculated by Manning's theory.
Two additional results are presented, which bear on the problem of toroidal ***DNA*** condensation.
Condensation occurs more readily at high temperatures.
Restriction fragments as short as 400 base-pairs form toroids by intermolecular condensation, which are similar in diameter and appearance to the intramolecular condensates formed by λ DNA.

L6 ANSWER 95 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 69
ACCESSION NUMBER: 1980:71278 CAPLUS Full-text
DOCUMENT NUMBER: 92:71278
TITLE: Thermodynamic stability theory for DNA doughnut shapes induced by charge neutralization
AUTHOR(S): Manning, Gerald S.
CORPORATE SOURCE: Dep. Chem., Rutgers, State Univ., New Brunswick, NJ, 08903, USA
SOURCE: Biopolymers (1980), 19(1), 37-59
CODEN: BIPMAA; ISSN: 0006-3525
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
A thermodn. anal. of the bending free energy of DNA, initiated previously, was extended. The ionic-strength dependence of the persistence length of DNA in aqueous NaCl could be understood by postulating: (1) a rigid-rod 60 base-pair unit and (2) a neg. contribution from nonelectrostatic sources to the bending free energy of this unit. On electrostatic neutralization of the phosphate charge, the latter term alone survived, and bending became a spontaneous process. It was demonstrated from a theor. anal. of the ionic-strength dependence of the rate of denaturation of ***DNA*** that the above statements are restricted in their validity to radii of curvature >170 Å; beyond this limit, the steeply rising repulsive energy of tightly packed atoms dominates the bending free energy. Therefore, spontaneous bending on charge neutralization proceeds up to, but not beyond, this barrier to curvature. Doughnut forms of DNA induced by ***binding*** of cationic spermidine, spermine, or mixts. of Mg2+ and ***polyamines*** possessed maximum curvatures, corresponding to the radius of the hole in the middle, in the range 1/150-1/200 Å.

L6 ANSWER 96 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 70
ACCESSION NUMBER: 1977:479870 CAPLUS Full-text
DOCUMENT NUMBER: 87:79870
TITLE: A mechanism for the entrapment of DNA at an air-water interface
AUTHOR(S): Eickbush, Thomas H.; Moudrianakis, Evangelos N.
CORPORATE SOURCE: Dep. Biol., Johns Hopkins Univ., Baltimore, MD, USA
SOURCE: Biophysical Journal (1977), 18(3), 275-88
CODEN: BIOJAU; ISSN: 0006-3495
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Addition of the intercalating dye quinacrine to a low-ionic-strength solution of DNA in quantities sufficient to saturate the high affinity sites in the DNA results in the accumulation of the DNA at the solution interface. This entrapment was assayed by the adsorption of DNA to untreated C-coated electron microscope grids touched to the solution surface. Other intercalating dyes can also bring about this entrapment, if they possess a side arm large enough to occupy one of the DNA grooves when the dye is intercalated into the DNA. The extension and unwinding of the DNA helix brought about by the ***intercalating*** chromophore of the dye mols. are not requirements for the entrapment process. Spermidine, a simple polyamine that will ***bind*** to the DNA minor groove but that has no intercalating chromophore, also causes this entrapment. Even simple mono- and divalent cations in the absence of the above ligands promote a low level of surface entrapment. A model for the entrapment of DNA at the air-water interface is proposed in which 1 (or both) of the hydrophobic grooves of the DNA becomes a surface-active agent as a consequence of the association of various ligands and charge neutralization.

L6 ANSWER 97 OF 98 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1967:460901 CAPLUS Full-text
DOCUMENT NUMBER: 67:60901
TITLE: Frameshift mutations and the genetic code
AUTHOR(S): Streisinger, George; Okada, Yoshimi; Emrich, Joyce; Newton, Judith; Tsugita, Akira; Terzaghi, Eric; Inouye, Masayori
CORPORATE SOURCE: Univ. of Oregon, Eugene, OR, USA
SOURCE: Cold Spring Harbor Symposia on Quantitative Biology (1967), Volume Date 1966, 31, 77-84
CODEN: CSHSAZ; ISSN: 0091-7451
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
A frameshift mutation may occur as the result of a gap in one of the two chains of a DNA mol. at or near a region of a repeating set of bases. There may then be a mispairing of bases at the repeating sequence, and a new synthesis filling the gap with an addition or deletion of a base or bases. The frequency of frameshift mutation is expected to be highest in longer stretches of identical bases. A particular mechanism is proposed for frameshift mutations in phage T4. It is also proposed that acridines intercalated between base pairs in the regions of mispairing increase the half life of the H-bonding of those regions and thereby increase the probability of synthesis occurring before the regions melt out. Proflavine and similar acridines are highly mutagenic in phage T4 but are not mutagenic in several strains of bacteria. Acridines or acridinelike substances with half-mustard or polyamine side chains are highly mutagenic in bacteria and other organisms. It is suggested that the mechanism of mutagenesis in bacteria may be similar to that proposed for phage T4, except that the mispairing and new synthesis would occur at the site of a mutagen-induced break. 22 references.

L6 ANSWER 98 OF 98 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1998:485627 BIOSIS Full-text
DOCUMENT NUMBER: PREV199800485627
TITLE: Progress in the design of DNA sequence-specific lexitropsins.
AUTHOR(S): Walker, Wynn L.; Kopka, Mary L.; Goodsell, David S. [Reprint author]
CORPORATE SOURCE: Dep. Mol. Biol., Scripps Res. Inst., La Jolla, CA 92037, USA
SOURCE: Biopolymers, (Sept. 28, 1997 (1998)) Vol. 44, No. 4, pp. 323-334. print.
CODEN: BIPMAA. ISSN: 0006-3525.
DOCUMENT TYPE: Article
General Review; (Literature Review)
LANGUAGE: English
ENTRY DATE: Entered STN: 5 Nov 1998
Last Updated on STN: 5 Nov 1998
ABSTRACT:
Sequence-specific polyamides that bind in the minor ***groove*** of DNA are attractive candidates for antibiotics, cancer chemotherapeutics, and transcriptional antagonists. This paper reviews the progress of structure-based design of minor ***groove*** -binding polyamides, from the first structure of netropsin with DNA, to the effective linked polyamides currently under study. A theory of polyamide specificity is also reviewed, introducing methods to determine the optimal strategies for targeting a given DNA sequence within a genome of competing sequences.

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FILE 'CAPLUS, BIOSIS, EMBASE, SCISEARCH' ENTERED AT 08:54:42 ON 09 JUN 2004

INDEX 'CAPLUS, BIOSIS, EMBASE, SCISEARCH' ENTERED AT 08:54:59 ON 09 JUN 2004

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264 FILE CAPLUS
138 FILE BIOSIS
140 FILE EMBASE
188 FILE SCISEARCH
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L3 ANALYZE PLU=ON L2 1-730 PD : 355 TERMS
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SET LINE 250
SET DETAIL OFF
SET LINE LOGIN
SET DETAIL LOGIN
L4 486 SEA PLU=ON L2 AND PY>=1999
L5 244 SEA PLU=ON L2 NOT L4
L6 98 DUP REM L5 (146 DUPLICATES REMOVED)
L*** DEL ANALYZE L5 1- PD : 81 TERMS
D FBIB ABS HITSTR TOTAL
SET LINE 250
SET DETAIL OFF
SET LINE LOGIN
SET DETAIL LOGIN
L*** DEL 98 FOCUS L6 1-
D RANK
D L6 1-98 IBIB IABS

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